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<u>AMEND THIS APPLICATION AS FOLLOWS</u> (By entering the complete listing of the claims below):

Claims 1-568 (PREVIOUSLY CANCELED).

Claim 569 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising:

providing a nucleic acid of interest;

providing or generating detectable non-radioactively labeled non-radioactive nucleic acid fragments, each fragment comprising: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof, and (b) one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, provided that said nucleotide analogs can be incorporated within, or onto a terminus of, said fragments without substantially interfering with the ability of said fragments to hybridize to the nucleic acid of interest or portion thereof which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof;

subjecting said fragments to a sequencing gel to separate or resolve said fragments; detecting non-radioactively the presence of each of said separated or resolved fragments by detecting the modified or labeled nucleotides or <a href="mailto:the modified or labeled">the modified or labeled</a> nucleotide analogs that are incorporated within, or onto a terminus of, said fragments; and

determining the sequence of said nucleic acid of interest.

Claim 570 (CURRENTLY AMENDED). The process according to claim 569, wherein the said nucleic acid sequence of interest is derived from an organism.

Claim 571 (CURRENTLY AMENDED). The process according to claim 570, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

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Claim 572 (CANCELED).

Claim 573 (CURRENTLY AMENDED). The process according to claim 572 571, wherein said mammal comprises a human being mammals comprise human beings.

Claim 574 (PREVIOUSLY PRESENTED). The process according to claim 570, wherein said organism is living.

Claim 575 (CURRENTLY AMENDED). The process according to claims 570 or 574, wherein said organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 576 (CANCELED).

Claim 577 (CURRENTLY AMENDED). The process according to claim 576 575, wherein said eukaryotic nucleic acid sequence of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 578 (CANCELED).

Claim 579 (CANCELED).

Claim 580 (CANCELED).

Claim 581 (CANCELED).

Claim 582 (CURRENTLY AMENDED). The process according to claim 581 577, wherein said human mammalian chromosomal nucleic acid sequence of interest comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

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Claim 583 (CURRENTLY AMENDED). The process according to claim 569, wherein said modified or labeled nucleotides or <u>said modified or labeled</u> nucleotide analogs are incorporated within, or onto a terminus of, said fragments with an enzyme.

Claim 584 (CURRENTLY AMENDED). The process according to claim 583, wherein said modified or labeled nucleotides or <u>said modified or labeled</u> nucleotide analogs comprise nucleoside triphosphates selected from the group consisting of <u>which comprise</u> ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and <u>or</u> a combination of any of the foregoing.

Claim 585 (PREVIOUSLY PRESENTÉD). The process according to claim 569, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Claim 586 (CURRENTLY AMENDED). The process according to claim 569, wherein the detectable non-radioactively labeled non-radioactive nucleic acid fragments hybridize to the nucleic acid of interest or to a portion thereof prior to separation in said sequencing gel.

Claim 587 (CURRENTLY AMENDED). The process according to claim 569, wherein before or during said providing or generating step, at least one of the modified or labeled nucleotides or the modified or labeled nucleotide analogs are incorporated at a terminus of at least one of said fragments.

Claim 588 (CURRENTLY AMENDED). The process according to claim 583, wherein at least one of said modified or labeled nucleotides or <u>said modified or labeled</u> nucleotide analogs is incorporated <u>by an enzyme</u> at a terminus of at least one of said fragments.

Claim 589 (CURRENTLY AMENDED). The process according to claim 588, wherein said enzyme is comprises a terminal transferase, a ligase or a polymerase.

Claim 590 (CANCELED).

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Claim 591 (CANCELED).

Claim 592 (CURRENTLY AMENDED). The process according to claim 569, wherein at least one of said modified or labeled nucleotides or <u>said modified or labeled</u> nucleotide analogs is incorporated onto a terminus of said fragments through chemical coupling.

Claim 593 (PREVIOUSLY PRESENTED). The process according to claim 592, wherein said chemical coupling is carried out with carbodiimide or formaldehyde.

Claim 594 (CURRENTLY AMENDED). The process according to claim 587, 588 or 592, wherein said terminus is a 3' terminus or a 5' terminus.

Claim 595 (CANCELED).

Claim 596 (PREVIOUSLY CANCELED).

Claim 597 (CURRENTLY AMENDED). The process according to claim 569 or 596, wherein, said incorporation is carried out by means of a polymerizing enzyme.

Claim 598 (CURRENTLY AMENDED). The process according to claim <u>597</u>, wherein said polymerizing enzyme comprises a polymerase.

Claim 599 (CURRENTLY AMENDED). The process according to claim 598, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 600 (CURRENTLY AMENDED). The process according to claim 569, wherein at said providing or generating step, the modified or labeled nucleotides or <u>the modified or labeled</u>

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nucleotide analogs comprise one or more members structures selected from the group consisting of one or more of which comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

#### wherein

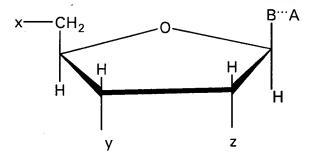
PM is a phosphate moiety,

SM is a furanose <u>furanosyl</u> moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7 deazapurine moiety;



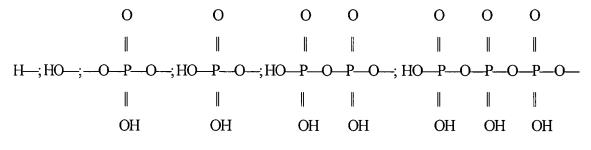
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

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# wherein B and A are covalently attached directly or through a linkage group; and

#### wherein x comprises:



## wherein y comprises:

## wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula

#### wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety, and

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wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 601 (CANCELED).

Claim 602 (CURRENTLY AMENDED). The process according to claim 601 600, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 603 (CURRENTLY AMENDED). The process according to claim 600, wherein PM is selected from the group consisting of comprises a mono-phosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

Claim 604 (CURRENTLY AMENDED). The process according to claim 600, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 605 (CANCELED).

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Claim 606. (CANCELED).

Claim 607 (CURRENTLY AMENDED). The process according to claim 600, wherein SM is selected from the group consisting of comprises ribose, deoxyribose and or dideoxyribose.

Claim 608 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>B in said</u> nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide <u>structure</u> or nucleotide analog structure (ii), (ii) or (iii) is <u>comprises</u> a 7-deazapurine.

Claim 609 (PREVIOUSLY CANCELED).

Claim 610 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>in</u> said modified or labeled nucleotides or nucleotide analogs comprise nucleotide <u>structure</u> or nucleotide analog structure (i), and Sig in said nucleotide or nucleotide analog structure (i) A is covalently attached to B at a position when B is a pyrimidine that is selected from the group consisting of the <u>C5 position</u>, the C2 position, the N3 position, the C6 position, and or combinations thereof when B is a pyrimidine, or is covalently attached to B at a position, when B is a purine, that is selected from the group consisting of the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when B is a purine, or is covalently attached to B at the 7 position when the is a 7-deazapurine.

Claim 611 (CURRENTLY AMENDED). The process according to claim 600, wherein  $\frac{\text{Sig } A}{\text{Sig } A}$  in said nucleotide structure or nucleotide analog structure (i) is covalently attached to B at a position selected from the group consisting of comprising the N<sup>4</sup> position when said pyrimidine comprises cytosine, the N<sup>2</sup> position when said purine comprises adenine or deazaadenine, the N<sup>6</sup> position when said purine comprises guanine or deazaguanine, and or combinations thereof.

Claim 612 (CURRENTLY AMENDED). The process according to claim 606 600, wherein in said nucleotide <u>structure</u> or nucleotide analog structure (ii) <u>or (iii)</u>, PM is attached to SM at a <u>position</u> independently selected from the group consisting of the 2', 3', and 5' positions, or any combination

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thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 613 (CANCELED).

Claim 614 (CURRENTLY AMENDED) The process according to claim 600, wherein said covalent attachment in nucleotide <u>structure</u> or nucleotide analog structure (iii) <u>is selected from the group eonsisting of comprises</u>

and or

Claim 615 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>in said</u> nucleotide structure or nucleotide analog structure (iii) PM is <u>comprises</u> a mono-, di- or triphosphate, and wherein in said nucleotide <u>structure</u> or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 616 (CURRENTLY AMENDED). The process according to claim 600, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or

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(iii) does not interfere substantially with the characteristic ability of <u>A or</u> Sig to form a detectable non-radioactive signal.

Claim 617 (CURRENTLY AMENDED). The process according to claim 600, wherein, in nucleotide or nucleotide analog structure (i), said covalent attachment comprises a member selected from the group consisting of: a — $CH_2NH$ — moiety, an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or both.

Claim 618 (CURRENTLY AMENDED). The process according to claim 600, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 619 (CURRENTLY AMENDED). The process according to claim 600, wherein in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or any of the moieties

$$--CH = CH_{2}--NH--,$$

$$--CH = CH--CH_{2}--NH--,$$

$$--CH = CH--CH_{2}--O--CH_{2}--CH--NH--,$$

$$O$$

$$O$$

$$||$$

$$--S--, --C--O, and or --O--.$$

Claim 620 (CURRENTLY AMENDED). The process according to claim 600, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment <u>includes comprises</u> a glycosidic linkage moiety.

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Claim 621 (CURRENTLY AMENDED). The process according to claim 600, wherein in any of said nucleotide <u>structure</u> or nucleotide analog structure (i), <u>said A is covalently attached to B</u> through a linkage group, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), said Sig is covalently attached to <del>BASE</del>, SM or PM through a linkage group.

Claim 622 (CURRENTLY AMENDED). The process according to claim 621, wherein, in nucleotide or nucleotide analog structure (i), said linkage group contains comprises an amine.

Claim 623 (PREVIOUSLY PRESENTED). The process according to claim 622, wherein said amine comprises a primary amine.

Claim 624 (PREVIOUSLY PRESENTED). The process according to claim 621, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 625 (CANCELED).

Claim 626 (CANCELED).

Claim 627 (CANCELED).

Claim 628 (CANCELED).

Claim 629 (CANCELED).

Claim 630 (CANCELED).

Claim 631 (CANCELED).

Claim 632 (CANCELED).

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Claim 633 (CANCELED).

Claim 634 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A</u> comprises more than three carbon atoms or said Sig comprises at least three carbon atoms.

Claim 635 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A or said</u> Sig comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 636 (CANCELED).

Claim 637 (CURRENTLY AMENDED). The process according to claim 600, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

Claim 638 (PREVIOUSLY PRESENTED). The process according to claim 637, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 639 (CANCELED).

Claim 640 (CANCELED).

Claim 641 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A or said Sig comprises</u> a monosaccharide, polysaccharide or an oligosaccharide.

Claim 642 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A or said</u> Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic

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component, a chemiluminescent component, an antigen, a hapten, an antibody component or a chelating component or a combination of any of the foregoing.

Claim 643 (CANCELED).

Claim 644 (PREVIOUSLY CANCELED).

Claim 645 (CANCELED).

Claim 646 (CURRENTLY AMENDED). The process according to claim 645 642, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 647 (PREVIOUSLY CANCELED).

Claim 648 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A or said</u> Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 649 (PREVIOUSLY PRESENTED). The process according to claim 648, wherein the binding protein comprises a lectin.

Claim 650 (PREVIOUSLY PRESENTED). The process according to claim 649, wherein the lectin comprises concanavalin A.

Claim 651 (PREVIOUSLY PRESENTED). The process according to claim 649, wherein said lectin is conjugated to ferritin.

Claim 652 (PREVIOUSLY CANCELLED).

Claim 653 (PREVIOUSLY CANCELLED).

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Claim 654 (CANCELED).

Claim 655 (CANCELED).

Claim 656 (CURRENTLY AMENDED). The process according to claim 655 642, wherein said metal-containing component is catalytic.

Claim 657 (CURRENTLY AMENDED). The process according to claim 600, wherein <u>said A or said Sig comprises is a non-radioactively detectable indicator moiety molecule.</u>

Claim 658 (CURRENTLY AMENDED). The process according to claim 657, wherein said indicator <del>moiety</del> molecule comprises an aromatic structure.

Claim 659 (PREVIOUSLY PRESENTED). The process according to claim 658, wherein said aromatic structure is heterocyclic.

Claim 660 (PREVIOUSLY PRESENTED). The process according to claim 659, wherein said heterocyclic aromatic structure is fluorescent.

Claim 661 (CURRENTLY AMENDED). The process according to claim 660, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 662 (CANCELED).

Claim 663 (CANCELED).

Claim 664 (CANCELED).

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Claim 665 (CANCELED).

Claim 666 (CANCELED).

Claim 667 (CURRENTLY AMENDED). The process according to claim 642, wherein <u>said A or said</u> Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claim 668 (CANCELED).

Claim 669 (CANCELED).

Claim 670 (CURRENTLY AMENDED). The process according to claim 657, wherein said indicator moiety molecule comprises a member selected from the group consisting of comprising a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and or a combination of any of the foregoing.

Claim 671 (CANCELED).

Claim 672 (CANCELED).

Claim 673 (CANCELED).

Claim 674 (CANCELED).

Claim 675 (CANCELED).

Claim 676 (CANCELED).

Claim 677 (CANCELED).

Page 18 [Supplemental Amendment To Applicants' December 31, 2003 Amendment -July 13, 2004] Claim 678 (CANCELED). Claim 679 (CANCELED). Claim 680 (PREVIOUSLY CANCELED) Claim 681 (CANCELED). Claim 682 (CANCELED). Claim 683 (PREVIOUSLY CANCELED). Claim 684 (CANCELED). Claim 685 (CANCELED). Claim 686 (CANCELED). Claim 687 (CANCELED). Claim 688 (PREVIOUSLY CANCELED). Claim 689 (PREVIOUSLY CANCELED). Claim 690 (CANCELED). Claim 691 (CANCELED). Claim 692 (CANCELED).

Enz-5(D8)(C2)

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Page 19 [Supplemental Amendment To Applicants' December 31, 2003 Amendment – July 13, 2004] Claim 693 (CANCELED). Claim 694 (CANCELED). Claim 695 (CANCELED). Claim 696. (CANCELED). Claim 697 (CANCELED). Claim 698 (CANCELED). Claim 699 (CANCELED). Claim 700 (CANCELED). Claim 701 (CANCELED). Claim 702 (CANCELED). Claim 703 (CANCELED). Claim 704 (CANCELED). Claim 705 (CANCELED). Claim 706 (CANCELED).

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Claim 707 (CURRENTLY AMENDED). The process according to claim 569, wherein said labeled detectable non-radioactive nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of comprising a fluorescent measurement, a chemiluminescent measurement, and or a combination thereof.

Claim 708 (PREVIOUSLY PRESENTED). The process according to claim 569, wherein said subjecting step is carried out electrophoretically.

Claim 709 (CURRENTLY AMENDED). The process according to claims 569, or 600 or 601, wherein said detecting step is carried out directly.

Claim 710 (CURRENTLY AMENDED). The process according to claim 709, wherein the labeled detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator moieties molecules and said direct detection is carried out using these indicator moieties molecules.

Claim 711 (CURRENTLY AMENDED). The process according to claim 710, wherein said non-radioactively detectable indicator moieties molecules comprise fluorescently labeled nucleotides.

Claim 712 (PREVIOUSLY PRESENTED). The process according to claim 711, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 713 (CURRENTLY AMENDED). The process according to claim 709, wherein said detecting step is carried out by means of a directly detectable signal provided by said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs, A or Sig.

Claim 714 (CURRENTLY AMENDED). The process according to claim 713, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating structure, a fluorogenic structure, a chromogenic structure, a chemiluminescent structure and or an electron dense structure.

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Claim 715 (PREVIOUSLY CANCELED).

Claim 716 (CURRENTLY AMENDED). The process according to claims claim 600-or 601, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said modified or labeled nucleotides or modified or labeled nucleotide analogs, A or Sig.

Claim 717 (CURRENTLY AMENDED). The process according to claim 716, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of comprises an antibody, an antigen, a hapten, a receptor, a ligand and or an enzyme.

Claim 718 (PREVIOUSLY CANCELED).

Claim 719 (CURRENTLY AMENDED). The process according to claim 569, wherein said detectable non-radioactively modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs are capable of being detected non-radioactively by a member selected from the group eonsisting of <u>comprising</u> an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and <u>or</u> an electron density measurement.

Claim 720 (CURRENTLY AMENDED). The process according to claim 569, wherein said detecting step comprises localizing said non-radioactively labeled nucleic acid fragments by means of said detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 721 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising:

providing a nucleic acid of interest;

providing or generating detectable non-radioactive nucleic acid fragments that are non-radioactively labeled, each fragment comprising: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof, and (b) one or more detectable non-radioactively modified or

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labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, provided that said modified or labeled nucleotide analogs can be attached to said fragments or incorporated within or onto a terminus of said fragments without substantially interfering with the ability of said fragments to hybridize to the nucleic acid of interest or portion thereof which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof;

introducing or subjecting said fragments to a sequencing gel; separating or resolving said fragments in said sequencing gel; detecting non-radioactively each of the separated or resolved fragments; and determining the sequence of said nucleic acid of interest.

Claim 722 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 723 (CURRENTLY AMENDED). The process according to claim 722, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 724 (CANCELED).

Claim 725 (CURRENTLY AMENDED). The process according to claim 724 723, wherein said mammal comprises a human being mammals comprise human beings.

Claim 726 (CURRENTLY AMENDED). The process according to claim 721 722, wherein said organism is living.

Claim 727 (CURRENTLY AMENDED). The process according to claims 722 or 726, wherein said organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

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Claim 728 (CANCELED).

Claim 729 (CURRENTLY AMENDED). The process according to claim 728 727, wherein said eukaryotic nucleic acid sequence of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 730 (CANCELED).

Claim 731 (CANCELED).

Claim 732 (CANCELED).

Claim 733 (CANCELED).

Claim 734 (CURRENTLY AMENDED). The process according to claim 733 729, wherein said human mammalian chromosomal nucleic acid sequence of interest comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 735 (CURRENTLY AMENDED). The process according to claim 721, wherein in said providing or generating step the fragments are provided or generated by one or more primers, or nucleoside triphosphates, or a combination thereof.

Claim 736 (CURRENTLY AMENDED). The process according to claim 735, wherein said nucleoside triphosphates are selected from the group consisting of comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and or a combination of any of the foregoing.

Claim 737 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

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Claim 738 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

Claim 739 (CURRENTLY AMENDED). The process according to claim 721, wherein at said providing or generating step, the modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

Claim 740 (CURRENTLY AMENDED). The process according to claim 739, wherein at least one of said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs is at a terminus <u>of at least one</u> of said <del>fragment or</del> fragments.

Claim 741 (PREVIOUSLY PRESENTED). The process according to claim 740, wherein said terminus comprises the 5' or the 3' terminus.

Claim 742 (PREVIOUSLY PRESENTED). The process according to claim 739, wherein said incorporation has been carried out in the presence of a primer.

Claim 743 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

Claim 744 (CURRENTLY AMENDED). The process according to claim 743, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 745 (CURRENTLY AMENDED). The process according to claim 721, wherein said nucleotide analog ean be <u>has been</u> coupled to DNA or RNA by a coupling means selected from the group consisting of comprising chemical coupling and <u>or</u> enzymatic coupling.

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Claim 746 (CURRENTLY AMENDED). The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group eonsisting of comprising carbodiimide and or formaldehyde.

Claim 747 (CURRENTLY AMENDED). The process according to claim 745, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of comprising DNA ligase and or RNA ligase.

Claim 748 (PREVIOUSLY CANCELED).

Claim 749 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 750 (PREVIOUSLY PRESENTED). The process according to claim 749, wherein said polymerizing enzyme comprises a polymerase.

Claim 751 (CURRENTLY AMENDED). The process according to claim 750, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 752 (CURRENTLY AMENDED). The process according to claim 721, wherein at said providing or generating step, the modified or labeled nucleotides or the modified or labeled nucleotide analogs comprise one or more structures members selected from the group consisting of which comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

PM SM BASE Sig

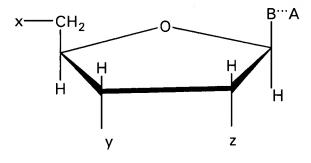
wherein

PM is a phosphate moiety, SM is a furanose moiety,

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BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety;



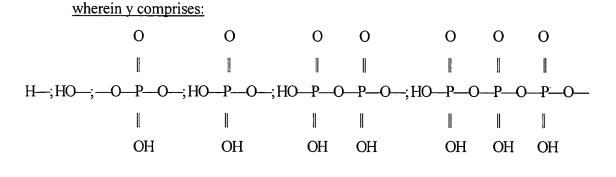
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

wherein B and A are covalently attached directly or through a linkage group; and

wherein x comprises:

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## wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

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BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 753 (CANCELED).

Claim 754 (CURRENTLY AMENDED). The process according to claim <del>753</del> 752, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 755 (CURRENTLY AMENDED). The process according to claim 721 752, wherein PM is selected from the group consisting of comprises a mono-phosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

Claim 756 (CURRENTLY AMENDED). The process according to claim 752, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 757 (CANCELED).

Claim 758. (CANCELED).

Claim 759 (CURRENTLY AMENDED). The process according to claim 721-or 752, wherein said furanose SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2', 3'- dideoxyribose.

Claim 760 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>B in said</u> nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide structure or nucleotide analog structure (ii), (ii) or (iii) is comprises a 7-deazapurine.

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Claim 761 (PREVIOUSLY CANCELED).

Claim 762 (CURRENTLY AMENDED). The process according to claim 752, wherein Sig A in said nucleotide or nucleotide analog structure (i) is covalently attached to BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C5 position, the C2 position, the N3 position, the C6 position, and or combinations thereof when B is a pyrimidine, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when B is a purine, or is covalently attached to B at the 7-position when B is a 7-deazapurine.

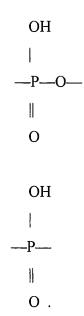
Claim 763 (CURRENTLY AMENDED). The process according to claim 752, wherein  $\underbrace{Sig\ A}$  in said nucleotide or nucleotide analog structure (i) is covalently attached to  $\underbrace{BASE\ B}$  at a position selected from the group consisting of comprising the  $N^4$  position when said pyrimidine comprises cytosine, the  $N^2$  position when said purine comprises adenine or deazaadenine, the  $N^6$  position when said purine comprises guanine or deazaguanine, and or combinations thereof.

Claim 764 (CURRENTLY AMENDED). The process according to claim 758 752, wherein in said nucleotide or nucleotide analog structure (ii) or (iii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' position, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 765 (CANCELED).

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Claim 766 (CURRENTLY AMENDED). The process according to claim 752, wherein said covalent attachment in nucleotide or nucleotide analog structure (iii) is selected from the group eonsisting of comprises:



Claim 767 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>in said</u> <u>nucleotide structure or nucleotide analog structure (iii)</u> PM is <u>comprises</u> a mono-, di or triphosphate, and wherein <u>in</u> said nucleotide <u>structure</u> or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 768 (CURRENTLY AMENDED). The process according to claim 752, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of <u>A or</u> Sig to form a detectable non-radioactive signal.

Claim 769 (CURRENTLY AMENDED). The process according to claim 752, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises a <u>member selected from the group consisting of:</u> a —CH<sub>2</sub>NH— moiety, an olefinic bond at the α-position

and or

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relative to the point of attachment to the nucleotide <u>structure or nucleotide analog structure (i)</u>, or both.

Claim 770 (CURRENTLY AMENDED). The process according to claim 752, wherein, in <u>said</u> nucleotide or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 771 (CURRENTLY AMENDED). The process according to claim 752, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises  $\theta r$  includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide <u>structure</u> or nucleotide analog structure (i), or any of the moieties

$$-CH = CH_2 - NH_-,$$
 $-CH = CH - CH_2 - NH_-,$ 
 $-CH = CH - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH = CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH = CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH$ 

Claim 772 (CURRENTLY AMENDED). The process according to claim 752, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment <u>includes comprises</u> a glycosidic linkage moiety.

Claim 773 (CURRENTLY AMENDED). The process according to claim 752, wherein in any of said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

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Claim 774 (CURRENTLY AMENDED). The process according to claim 773, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>eontains</u> <u>comprises</u> an amine.

Claim 775 (PREVIOUSLY PRESENTED). The process according to claim 774, wherein said amine comprises a primary amine.

Claim 776 (PREVIOUSLY PRESENTED). The process according to claim 773, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 777 (CANCELED).

Claim 778 (CANCELED).

Claim 779 (CANCELED). .

Claim 780 (CANCELED).

Claim 781 (CANCELED).

Claim 782 (CANCELED).

Claim 783 (CANCELED).

Claim 784 (CANCELED).

Claim 785 (CANCELED).

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Claim 786 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>said A comprises more than three carbon atoms and Sig comprises at least three carbon atoms.</u>

Claim 787 (CURRENTLY AMENDED). The process according to claim 752, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 788 (CANCELED).

Claim 789 (CURRENTLY AMENDED). The process according to claim 752, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

Claim 790 (PREVIOUSLY PRESENTED). The process according to claim 789, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 791 (CANCELED).

Claim 792 (CANCELED).

Claim 793 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>said A or</u> said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 794 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>said A or said</u> Sig comprises a <u>member selected from the group consisting of</u> biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component, or any combination of the foregoing.

Claim 795 (CANCELED).

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Claim 796 (CURRENTLY AMENDED). The process according to claim <del>795</del> <u>794</u>, wherein said electron dense component comprises ferritin.

Claim 797 (CURRENTLY AMENDED). The process according to claim 794, wherein Sig emprises a said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 798 (PREVIOUSLY CANCELED).

Claim 799 (PREVIOUSLY CANCELED).

Claim 800 (CURRENTLY AMENDED). The process according to claim 752, wherein <u>said A or said</u> Sig comprises a sugar residue and the <u>said</u> sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 801 (PREVIOUSLY PRESENTED). The process according to claim 800, wherein the binding protein comprises a lectin.

Claim 802 (PREVIOUSLY PRESENTED). The process according to claim 801, wherein the lectin comprises concanavalin A.

Claim 803 (PREVIOUSLY PRESENTED). The process according to claim 801, wherein said lectin is conjugated to ferritin.

Claim 804 (PREVIOUSLY CANCELED).

Claim 805 (PREVIOUSLY CANCELED).

Claim 806 (CANCELED).

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Claim 807 (CANCELED).

Claim 808 (CURRENTLY AMENDED). The process according to claim 807 794, wherein said metal-containing component is catalytic.

Claim 809. (CURRENTLY AMENDED) The process according to claim 752, wherein <u>said A or</u> said Sig <del>comprises</del> is a non-radioactively detectable indicator <del>moiety</del> molecule.

Claim 810 (CURRENTLY AMENDED). The process according to claim 809, wherein said indicator <del>moiety</del> molecule comprises an aromatic structure.

Claim 811 (PREVIOUSLY PRESENTED). The process according to claim 810, wherein said aromatic structure is heterocyclic.

Claim 812 (PREVIOUSLY PRESENTED). The process according to claim 811, wherein said heterocyclic aromatic structure is fluorescent.

Claim 813 (CURRENTLY AMENDED). The process according to claim 812, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 814 (CANCELED).

Claim 815 (CANCELED).

Claim 816 (CANCELED).

Claim 817 (CANCELED).

Claim 818 (CANCELED).

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Claim 819 (CURRENTLY AMENDED). The process according to claim 794, wherein <u>said A or said</u> Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claim 820 (CANCELED).

Claim 821 (CANCELED).

Claim 822 (CURRENTLY AMENDED). The process according to claim 809, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and or a combination of any of the foregoing.

Claim 823 (CANCELED).

Claim 824 (CANCELED).

Claim 825 (CANCELED).

Claim 826 (CANCELED).

Claim 827 (CANCELED).

Claim 828 (CANCELED).

Claim 829 (CANCELED).

Claim 830 (CANCELED).

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995) Page 37 [Supplemental Amendment To Applicants' December 31, 2003 Amendment – July 13, 2004] Claim 831 (CANCELED). Claim 832 (PREVIOUSLY CANCELED). Claim 833 (CANCELED). Claim 834 (CANCELED). Claim 835 (PREVIOUSLY CANCELED). Claim 836 (CANCELED). Claim 837 (CANCELED). Claim 838 (CANCELED). Claim 839 (CANCELED). Claim 840 (PREVIOUSLY CANCELED). Claim 841 (PREVIOUSLY CANCELED). Claim 842 (CANCELED). Claim 843 (CANCELED). Claim 844 (CANCELED). Claim 845 (CANCELED).

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Claim 846 (CANCELED).

Claim 847 (CANCELED).

Claim 848 (CANCELED).

Claim 849 (CANCELED).

Claim 850 (CANCELED).

Claim 851 (CANCELED).

Claim 852 (CANCELED).

Claim 853 (CANCELED).

Claim 854 (CANCELED).

Claim 855 (CANCELED).

Claim 856 (CANCELED).

Claim 857 (CANCELED).

Claim 858 (CANCELED).

Claim 859 (CURRENTLY AMENDED). The process according to claim 721, wherein said detectable non-radioactively labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of comprising a fluorescent measurement, a chemiluminescent measurement, and or a combination thereof.

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Claim 860 (PREVIOUSLY PRESENTED). The process according to claim 721, wherein said separating or resolving step is carried out electrophoretically.

Claim 861 (CURRENTLY AMENDED). The process according to claims 721, or 752 or 753, wherein said detecting step is carried out directly.

Claim 862 (CURRENTLY AMENDED). The process according to claim 861, wherein the labeled detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator moieties molecules and said direct detection is carried out using these indicator moieties molecules.

Claim 863 (CURRENTLY AMENDED). The process according to claim 862, wherein said non-radioactively detectable indicator moieties molecules comprise fluorescently labeled nucleotides.

Claim 864 (PREVIOUSLY PRESENTED). The process according to claim 863, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 865 (CURRENTLY AMENDED). The process according to claim 861, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 866 (CURRENTLY AMENDED). The process according to claim 865, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating structure, a fluorogenic structure, a chromogenic structure, a chemiluminescent structure and or an electron dense structure.

Claim 867 (PREVIOUSLY CANCELED).

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Claim 868 (CURRENTLY AMENDED). The process according to claims 721; or 752 or 753, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 869 (CURRENTLY AMENDED). The process according to claim 868, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of comprises an antibody, an antigen, a hapten, a receptor, a ligand and or an enzyme.

Claim 870 (PREVIOUSLY CANCELED).

Claim 871 (CURRENTLY AMENDED). The process according to claim 721, wherein said one or more modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs are capable of being detected by <u>means comprising a member selected from the group consisting of</u> an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 872 (CURRENTLY AMENDED). The process according to claim 721, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs.

Claim 873 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising:

## providing a nucleic acid of interest;

providing or generating detectable non-radioactive nucleic acid fragments that are non-radioactively labeled, each fragment comprising: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof and (b) one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA;

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detecting non-radioactively the detectable non-radioactive labeled nucleic acid fragments with a sequencing gel; and

determining the sequence of said nucleic acid of interest.

Claim 874 (PREVIOUSLY PRESENTED). The process according to claim 873, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 875 (CURRENTLY AMENDED). The process according to claim 874, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 876 (CANCELED).

Claim 877 (CURRENTLY AMENDED). The process according to claim 876 875, wherein said mammal comprises a human being mammals comprise human beings.

Claim 878 (PREVIOUSLY PRESENTED). The process according to claim 874, wherein said organism is living.

Claim 879 (CURRENTLY AMENDED). The process according to claims 874 or 878, wherein said organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 880 (CANCELED).

Claim 881 (CURRENTLY AMENDED). The process according to claim 880 879, wherein said eukaryotic nucleic acid sequence of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 882 (CANCELED).

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Claim 883 (CANCELED).

Claim 884 (CANCELED).

Claim 885 (CANCELED).

Claim 886 (CURRENTLY AMENDED). The process according to claim 885 881, wherein said human mammalian chromosomal nucleic acid sequence of interest comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 887 (CURRENTLY AMENDED). The process according to claim 873, wherein in said providing or generating step, the fragments are provided or generated by one or more primers, nucleoside triphosphates, or a combination thereof.

Claim 888 (CURRENTLY AMENDED). The process according to claim 887, wherein said nucleoside triphosphates are selected from the group consisting of comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, and dideoxyribonucleoside triphosphates, and or a combination of any of the foregoing.

Claim 889 (PREVIOUSLY PRESENTED). The process according to claim 873, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Claim 890 (PREVIOUSLY PRESENTED). The process according to claim 873, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented and separated prior to detecting in said sequencing gel.

Claim 891. (CURRENTLY AMENDED). The process according to claim 873, wherein in said providing or generating step, the one or more modified or labeled nucleotides <u>or modified or labeled nucleotide analogs</u> have been incorporated into said nucleic acid fragment or fragments.

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Claim 892 (CURRENTLY AMENDED). The process according to claim 891, wherein at least one of said modified or labeled nucleotides or modified or labeled nucleotide analogs is at a terminus of at least one of said fragment or fragments.

Claim 893 (PREVIOUSLY PRESENTED). The process according to claim 892, wherein said terminus comprises the 5' or the 3' terminus.

Claim 894 (PREVIOUSLY PRESENTED). The process according to claim 891, wherein said incorporation has been carried out in the presence of a primer.

Claim 895 (CURRENTLY AMENDED). The process according to claim 873, wherein said modified or labeled nucleotide or modified or labeled nucleotide analog can be has been attached terminally to DNA or RNA by means of an enzyme.

Claim 896. (CURRENTLY AMENDED). The process according to claim 895, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 897 (CURRENTLY AMENDED). The process according to claim 873, wherein said nucleotide <u>analog ean be has been coupled</u> to DNA or RNA by a coupling means <del>selected from the group consisting of comprising chemical coupling and or enzymatic coupling.</del>

Claim 898 (CURRENTLY AMENDED). The process according to claim 897, wherein said chemical coupling ean be <u>has been</u> carried out by a chemical coupling means selected from the group consisting of comprising carbodiimide and <u>or</u> formaldehyde.

Claim 899 (CURRENTLY AMENDED). The process according to claim 898, wherein said enzymatic coupling ean be has been carried out by an enzymatic coupling means selected from the group consisting of comprising DNA ligase and or RNA ligase.

Claim 900 (PREVIOUSLY CANCELED).

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Claim 901 (PREVIOUSLY PRESENTED). The process according to claim 873, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 902 (CURRENTLY AMENDED). The process according to claim 901, wherein said polymerizing enzyme comprises a polymerase and the modified or labeled nucleotide or modified or labeled nucleotide analog is incorporated at a 3' terminus.

Claim 903 (CURRENTLY AMENDED). The process according to claim 902, wherein said polymerizing enzyme is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 904 (CURRENTLY AMENDED). The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or the modified or labeled nucleotide analogs comprise one or more nucleotide structures selected from the group consisting of one or more of structures which comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

#### wherein

PM is a phosphate moiety,

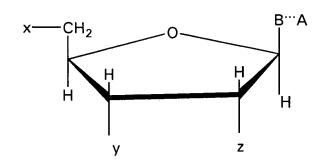
SM is a furanose moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

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wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

wherein B and A are covalently attached directly or through a linkage group;

and

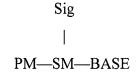
## wherein x comprises:

# wherein y comprises:

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## wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula



#### wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

#### wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 905 (CANCELED).

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Claim 906 (CURRENTLY AMENDED). The process according to claim 905 904, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 907 (CURRENTLY AMENDED). The process according to claim 873 904, wherein PM is selected from the group consisting of comprises a mono-phosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

Claim 908 (CURRENTLY AMENDED). The process according to claim 904, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 909 (CANCELED).

Claim 910 (CANCELED).

Claim 911 (CURRENTLY AMENDED). The process according to claim 904, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2', 3'-dideoxyribose.

Claim 912 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>B in said</u> nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide structures (i), (ii) or (iii) is comprises a 7-deazapurine.

Claim 913 (CANCELED).

Claim 914 (CURRENTLY AMENDED). The process according to claim 904, wherein Sig A in said nucleotide structure or nucleotide analog structure (i) is covalently attached to BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C5 position, the C2 position, the N3 position, the C6 position, and or combinations thereof when B is a pyrimidine, or is covalently attached to BASE at a position when BASE is a purine that is selected

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from the group consisting of the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when B is a purine, or is covalently attached to the 7-position when B is a 7-deazapurine.

Claim 915 (CURRENTLY AMENDED). The process according to claim 904, wherein  $\underbrace{\text{Sig A}}_{\text{Sig A}}$  in said nucleotide structure or nucleotide analog structure (i) is covalently attached to  $\underbrace{\text{BASE B}}_{\text{ASE B}}$  at a position selected from the group consisting of comprising the N<sup>4</sup> position when said pyrimidine comprises cytosine, the N<sup>2</sup> position when said purine comprises adenine or deazaadenine, the N<sup>6</sup> position when said purine comprises guanine or deazaguanine, and or combinations thereof.

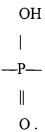
Claim 916 (CURRENTLY AMENDED). The process according to claim 910 904, wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 917 (CANCELED).

Claim 918 (CURRENTLY AMENDED). The process according to claim 904, wherein said covalent attachment in nucleotide structure or nucleotide analog structure (iii) is selected from the group consisting of comprises

and or

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Claim 919 (CURRENTLY AMENDED). The process according to claim 904, wherein in said nucleotide structure or nucleotide analog structure PM is comprises a mono-, di- or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 920 (CURRENTLY AMENDED). The process according to claim 904, wherein said covalent attachment in any of <u>said</u> nucleotide structure<u>s or nucleotide analog structures</u> (i), (ii) or (iii) does not interfere substantially with the characteristic ability of <u>A or</u> Sig to form a detectable non-radioactive signal.

Claim 921 (CURRENTLY AMENDED). The process according to claim 904, wherein, in nucleotide structure <u>or nucleotide analog structure</u> (i), said covalent attachment comprises a member selected from the group consisting of: a —CH<sub>2</sub>NH— moiety, an olefinic bond at the α-position relative to the point of attachment to the nucleotide structure <u>or nucleotide analog structure</u> (i), or both.

Claim 922 (CURRENTLY AMENDED). The process according to claim 904, wherein, in <u>said</u> nucleotide structure <u>or nucleotide analog structure</u> (i), said covalent attachment comprises an allylamine group.

Claim 923 (CURRENTLY AMENDED). The process according to claim 904, wherein, in <u>said</u> nucleotide structure <u>or nucleotide analog structure</u> (i), said covalent attachment comprises or

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includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide structure (i), or any of the moieties

$$-CH = CH_2 - NH_-$$
,
 $-CH = CH - CH_2 - NH_-$ ,
 $-CH = CH - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH = CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2$ ,
 $-CH_$ 

Claim 924 (CURRENTLY AMENDED). The process according to claim 904, wherein, in <u>said</u> nucleotide structure <u>or nucleotide analog structure</u> (i), said covalent attachment <u>includes comprises</u> a glycosidic linkage moiety.

Claim 925 (CURRENTLY AMENDED). The process according to claim 904, wherein in any of said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 926 (CURRENTLY AMENDED). The process according to claim 925, wherein, in nucleotide structure (i), said linkage group contains comprises an amine.

Claim 927 (PREVIOUSLY PRESENTED). The process according to claim 926, wherein said amine comprises a primary amine.

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Claim 928 (PREVIOUSLY PRESENTED). The process according to claim 925, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 929 (CANCELED).

Claim 930 (CANCELED).

Claim 931 (CANCELED).

Claim 932 (CANCELED).

Claim 933 (CANCELED).

Claim 934 (CANCELED).

Claim 935 (CANCELED).

Claim 936 (CANCELED).

Claim 937 (CANCELED).

Claim 938 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>said A comprises more than three carbon atoms and</u> Sig comprises at least three carbon atoms.

Claim 939 (CURRENTLY AMENDED). The process according to claim 904, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 940 (CANCELED).

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Claim 941 (CURRENTLY AMENDED). The process according to claim 904, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

Claim 942 (PREVIOUSLY PRESENTED). The process according to claim 941, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 943 (CANCELED).

Claim 944 (CANCELED).

Claim 945 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>said A or said</u> Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 946 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>said A or said Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component <u>or any combination of any of the foregoing</u>.</u>

Claim 947 (CURRENTLY AMENDED). The process according to claim 946, wherein Sig comprises an said electron dense component comprises ferritin.

Claim 948 (PREVIOUSLY CANCELED).

Claim 949 (CURRENTLY AMENDED). The process according to claim 946, wherein Sig eomprises a said magnetic component comprises magnetic oxide or magnetic iron oxide.

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Claim 950 (CANCELED).

Claim 951 (PREVIOUSLY CANCELED).

Claim 952 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>said A or said</u> Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 953 (PREVIOUSLY PRESENTED). The process according to claim 952, wherein the binding protein comprises a lectin.

Claim 954 (PREVIOUSLY PRESENTED). The process according to claim 953, wherein the lectin comprises concanavalin A.

Claim 955 (PREVIOUSLY PRESENTED). The process according to claim 953, wherein said lectin is conjugated to ferritin.

Claim 956 (PREVIOUSLY CANCELED).

Claim 957 (PREVIOUSLY CANCELED).

Claim 958 (CANCELED).

Claim 959 (CANCELED).

Claim 960 (CURRENTLY AMENDED) The process according to claim 959 946, wherein said metal-containing component is catalytic.

Claim 961 (CURRENTLY AMENDED). The process according to claim 904, wherein <u>said A or said Sig comprises is</u> a non-radioactively detectable indicator <u>moiety molecule</u>.

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Claim 962 (CURRENTLY AMENDED). The process according to claim 961, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 963 (PREVIOUSLY PRESENTED). The process according to claim 962, wherein said aromatic structure is heterocyclic.

Claim 964 (PREVIOUSLY PRESENTED). The process according to claim 963, wherein said heterocyclic aromatic structure is fluorescent.

Claim 965 (CURRENTLY AMENDED). The process according to claim 904, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 966 (CANCELED).

Claim 967 (CANCELED).

Claim 968 (CANCELED).

Claim 969 (CANCELED).

Claim 970 (CANCELED).

Claim 971 (CURRENTLY AMENDED) The process according to claim 946, wherein <u>said A or said</u> Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claim 972 (CANCELED).

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Claim 973 (CANCELED).

Claim 974 (CURRENTLY AMENDED). The process according to claim 961, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and or a combination of any of the foregoing.

Claim 975 (CANCELED).

Claim 976 (CANCELED).

Claim 977 (CANCELED).

Claim 978 (CANCELED).

Claim 979 (CANCELED).

Claim 980 (CANCELED).

Claim 981 (CANCELED).

Claim 982 (CANCELED).

Claim 983 (CANCELED).

Claim 984 (PREVIOUSLY CANCELED).

Claim 985 (CANCELED).

Claim 986 (CANCELED).

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995) Page 56 [Supplemental Amendment To Applicants' December 31, 2003 Amendment – July 13, 2004] Claim 987 (PREVIOUSLY CANCELED). Claim 988 (CANCELED). Claim 989 (CANCELED). Claim 990 (CANCELED). Claim 991 (CANCELED). Claim 992 (PREVIOUSLY CANCELED). Claim 993 (PREVIOUSLY CANCELED). Claim 994 (CANCELED). Claim 995 (CANCELED). Claim 996 (CANCELED). Claim 997 (CANCELED). Claim 998 (CANCELED). Claim 999 (CANCELED). Claim 1000 (CANCELED). Claim 1001 (CANCELED).

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Claim 1002 (CANCELED).

Claim 1003 (CANCELED).

Claim 1004 (CANCELED).

Claim 1005 (CANCELED).

Claim 1006 (CANCELED).

Claim 1007 (CANCELED).

Claim 1008 (CANCELED).

Claim 1009 (CANCELED).

Claim 1010 (CANCELED).

Claim 1011 (CURRENTLY AMENDED). The process according to claim 873, wherein said detectable non-radioactive labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of comprising a fluorescent measurement, a chemiluminescent measurement, and or a combination thereof.

Claim 1012 (PREVIOUSLY PRESENTED). The process according to claim 873, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

Claim 1013 (CURRENTLY AMENDED). The process according to claims 873, or 904 or 905, wherein said detecting step is carried out directly.

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Claim 1014 (CURRENTLY AMENDED). The process according to claim 1013, wherein the labeled detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator moieties molecules and said direct detection is carried out using one or more of these indicator moieties molecules.

Claim 1015 (CURRENTLY AMENDED). The process according to claim 1014, wherein said one or more non-radioactively detectable indicator <u>moieties molecule</u> comprises fluorescently labeled nucleotides.

Claim 1016 (PREVIOUSLY PRESENTED). The process according to claim 1015, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1017 (CURRENTLY AMENDED). The process according to claim 1016, wherein said detecting step is carried out by means of a directly detectable signal provided by said A, Sig or modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1018 (CURRENTLY AMENDED). The process according to claim 1013, wherein <u>in</u> said detecting step the directly detectable signal comprises a <u>member selected from the group consisting</u> of a chelating structure, a fluorogenic structure, a chromogenic structure, a chemiluminescent structure and <u>or</u> an electron dense structure.

Claim 1019 (PREVIOUSLY CANCELED).

Claim 1020 (CURRENTLY AMENDED). The process according to claims 873, or 904 or 905, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said A, Sig or modified or labeled nucleotides or modified or labeled nucleotide analogs.

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Claim 1021 (CURRENTLY AMENDED). The process according to claim 1020, wherein <u>in</u> said detecting step the indirectly detectable signal <u>is selected from the group consisting of comprises</u> an antibody, an antigen, a hapten, a receptor, a ligand <u>and or</u> an enzyme.

Claim 1022 (PREVIOUSLY CANCELED).

Claim 1023 (CURRENTLY AMENDED). The process according to claim 873, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are capable of being detected by means comprising a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1024 (CURRENTLY AMENDED). The process according to claim 873, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1025 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising detecting non-radioactively with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments which have been resolved or separated by a sequencing gel, wherein each of said fragments comprises: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof; and (b) one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, provided that said modified or labeled nucleotide analogs can be enzymatically incorporated within, or onto a terminus of, said fragments which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof.

Claim 1026 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein the nucleic acid sequence of interest is derived from an organism.

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Claim 1027 (CURRENTLY AMENDED). The process according to claim 1026, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 1028 (CANCELED).

Claim 1029 (CURRENTLY AMENDED). The process according to claim 1028 1027, wherein said mammal comprises a human being mammals comprise human beings.

Claim 1030 (PREVIOUSLY PRESENTED). The process according to claim 1026, wherein said organism is living.

Claim 1031 (CURRENTLY AMENDED). The process according to claims 1026 or 1030, wherein said organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 1032 (CANCELED).

Claim 1033 (CURRENTLY AMENDED). The process according to claim 1032 1031, wherein said eukaryotic nucleic acid sequence of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 1034 (CANCELED).

Claim 1035 (CANCELED).

Claim 1036 (CANCELED).

Claim 1037 (CANCELED).

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Claim 1038 (CURRENTLY AMENDED). The process according to claim 1037 1033, wherein said human mammalian chromosomal nucleic acid sequence of interest comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 1039 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein prior to said detecting step, the fragments are provided or generated by one or more primers or nucleoside triphosphates, or a combination thereof.

Claim 1040 (CURRENTLY AMENDED). The process according to claim 1039, wherein said nucleoside triphosphates are selected from the group consisting of comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and or a combination of any of the foregoing.

Claim 1041 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Claim 1042 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

Claim 1043 (CURRENTLY AMENDED). The process according to claim 1025, wherein prior to said detecting step, the modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs have been incorporated into said fragments.

Claim 1044 (CURRENTLY AMENDED). The process according to claim 1043, wherein at least one of said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs is at a terminus of at least one of said fragments.

Claim 1045 (PREVIOUSLY PRESENTED). The process according to claim 1044, wherein said terminus comprises the 5' or the 3' terminus.

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Claim 1046 (PREVIOUSLY PRESENTED). The process according to claim 1043, wherein said incorporation has been carried out in the presence of a primer.

Claim 1047 (CURRENTLY AMENDED). The process according to claim 1025, wherein said modified or labeled nucleotide or modified or labeled nucleotide analog ean be has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1048 (CURRENTLY AMENDED). The process according to claim 1047, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 1049 (CURRENTLY AMENDED). The process according to claim 1025, wherein said nucleotide analog ean be has been coupled to DNA or RNA by a coupling means comprising selected from the group consisting of chemical coupling and or enzymatic coupling.

Claim 1050 (CURRENTLY AMENDED). The process according to claim 1049, wherein said chemical coupling ean be has been carried out by a chemical coupling means comprising selected from the group consisting of carbodiimide and or formaldehyde.

Claim 1051 (PREVIOUSLY PRESENTED). The process according to claim 1049, wherein said incorporation is carried out by a DNA ligase or RNA ligase.

Claim 1052 (PREVIOUSLY CANCELED).

Claim 1053 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1054 (CURRENTLY AMENDED). The process according to claim 1053, wherein said polymerizing enzyme comprises a polymerase and the <u>modified or labeled nucleotide or modified or labeled nucleotide analog is incorporated at terminus is a 3' terminus.</u>

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Claim 1055 (CURRENTLY AMENDED). The process according to claim 1054, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 1056 (CURRENTLY AMENDED). The process according to claim 1025, wherein in said detecting step, the modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs comprise one or more <u>nucleotide or nucleotide</u> analog structures selected from the group consisting of one or more of structures:

(i) a nucleotide <u>structure</u> or nucleotide analog structure having the formula

wherein

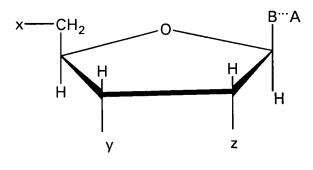
PM is a phosphate moiety,

SM is a furanose moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety;



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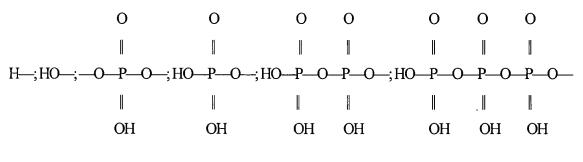
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

wherein B and A are covalently attached directly or through a linkage group;

<u>and</u>

## wherein x comprises:



wherein y comprises:

wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 1057 (CANCELED).

Claim 1058 (CURRENTLY AMENDED). The process according to claim 1057 1056, wherein in said nucleotide structure or nucleotide analog structure (i) y and z are H—.

Claim 1059 (CURRENTLY AMENDED). The process according to claim 1025, wherein PM is selected from the group consisting of comprises a mono-phosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

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Claim 1060 (CURRENTLY AMENDED). The process according to claim 1056, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 1061 (CANCELED).

Claim 1062. (CANCELED).

Claim 1063 (CURRENTLY AMENDED). The process according to claim 1025 or 1056, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2', 3'-dideoxyribose.

Claim 1064 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>B in said nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide or nucleotide analog structure (i), (ii) or (iii) is <u>comprises</u> a 7-deazapurine.</u>

Claim 1065 (PREVIOUSLY CANCELLED).

Claim 1066 (CURRENTLY AMENDED). The process according to claim 1056, wherein in Sig in said nucleotide structure or nucleotide analog structure (i), A is covalently attached to BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C5 position, the C2 position, the N3 position, the C6 position, and or combinations thereof when B is a pyrimidine, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when B is a purine, or is covalently attached to B the at a 7-position when B is a 7-deazapurine.

Claim 1067 (CURRENTLY AMENDED). The process according to claim 1056, wherein Sig A in said nucleotide or nucleotide analog structure (i) is covalently attached to BASE B at a position

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selected from the group consisting of comprising the  $N^4$  position when said pyrimidine comprises cytosine, the  $N^2$  position when said purine comprises adenine or deazaadenine, the  $N^6$  position when said purine comprises guanine or deazaguanine, and or combinations thereof.

Claim 1068 (CURRENTLY AMENDED). The process according to claim 1062, wherein in said nucleotide <u>structure</u> or nucleotide analog structure (ii) <u>or (iii)</u>, PM is attached to SM at a position independently <u>selected from the group consisting of comprising</u> the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1069 (CANCELED).

Claim 1070 (CURRENTLY AMENDED). The process according to claim 1056, wherein said covalent attachment in nucleotide <u>structure</u> or nucleotide analog structure (iii) is <u>selected from the group consisting of comprises</u>

and or

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Claim 1071 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>in said</u> <u>nucleotide structure or nucleotide analog structure (iii)</u> PM is <u>comprises</u> a mono-, di or triphosphate, and wherein <u>in said</u> nucleotide <u>structure</u> or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1072 (CURRENTLY AMENDED). The process according to claim 1056, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of <u>A or Sig</u> to form a detectable non-radioactive signal.

Claim 1073 (CURRENTLY AMENDED). The process according to claim 1056, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises a <u>member</u> selected from the group consisting of: a — $CH_2NH$ — moiety, an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or both.

Claim 1074 (CURRENTLY AMENDED). The process according to claim 1056, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

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Claim 1075 (CURRENTLY AMENDED). The process according to claim 1056, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises or includes: an olefinic bond at the α-position relative to the point of attachment to the nucleotide <u>structure</u> or nucleotide analog structure (i), or any of the moieties

$$-CH = CH_2 - NH_-,$$
 $-CH = CH - CH_2 - NH_-,$ 
 $-CH = CH - CH_2 - O - CH_2 - CH_- NH_-,$ 
 $OH$ 
 $O$ 
 $||$ 
 $-S-, -C-O, and -O-.$ 

Claim 1076 (CURRENTLY AMENDED). The process according to claim 1056, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment <u>includes</u> <u>comprises</u> a glycosidic linkage moiety.

Claim 1077 (CURRENTLY AMENDED). The process according to claim 1056, wherein in any of said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1078 (CURRENTLY AMENDED). The process according to claim 1077, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>contains</u> <u>comprises</u> an amine.

Claim 1079 (PREVIOUSLY PRESENTED). The process according to claim 1078, wherein said amine comprises a primary amine.

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Claim 1080 (PREVIOUSLY PRESENTED). The process according to claim 1077, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1081 (CANCELED).

Claim 1082 (CANCELED).

Claim 1083 (CANCELED).

Claim 1084 (CANCELED).

Claim 1085 (CANCELED).

Claim 1086 (CANCELED).

Claim 1087 (CANCELED).

Claim 1088 (CANCELED).

Claim 1089 (CANCELED).

Claim 1090 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>said A</u> <u>comprises</u> more than three carbon atoms and Sig comprises at least three carbon atoms.

Claim 1091 (CURRENTLY AMENDED). The process according to claim 1056, wherein said <u>A</u> or said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

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Claim 1092 (CANCELED).

Claim 1093 (CURRENTLY AMENDED). The process according to claim 1056, wherein said <u>A or said</u> Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

Claim 1094 (PREVIOUSLY PRESENTED). The process according to claim 1093, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1095 (CANCELED).

Claim 1096 (CANCELED).

Claim 1097 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>said A</u> or <u>said</u> Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1098 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>said A</u> <u>or said</u> Sig comprises a <u>member selected from the group consisting of</u> biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component <u>or any combination of the foregoing</u>.

Claim 1099 (CURRENTLY AMENDED). The process according to claim 1098, wherein Sig comprises said an electron dense component comprises ferritin.

Claim 1100 (PREVIOUSLY CANCELED).

Claim 1101 (CURRENTLY AMENDED). The process according to claim 1098, wherein Sig comprises a said magnetic component comprises magnetic oxide or magnetic iron oxide.

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Claim 1102 (CANCELED).

Claim 1103 (PREVIOUSLY CANCELED).

Claim 1104 (CURRENTLY AMENDED). The process according to claim 1056, wherein <u>said A</u> or <u>said</u> Sig comprises a sugar residue and <u>the said</u> the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 1105 (PREVIOUSLY PRESENTED). The process according to claim 1104, wherein the binding protein comprises a lectin.

Claim 1106 (PREVIOUSLY PRESENTED). The process according to claim 1105, wherein the lectin comprises concanavalin A.

Claim 1107 (PREVIOUSLY PRESENTED). The process according to claim 1105, wherein said lectin is conjugated to ferritin.

Claim 1108 (PREVIOUSLY CANCELED).

Claim 1109 (PREVIOUSLY CANCELED).

Claim 1110 (CANCELED).

Claim 1111 (CANCELED).

Claim 1112 (CURRENTLY AMENDED). The process according to claim 1111 1098, wherein said metal-containing component is catalytic.

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Claim 1113 (CURRENTLY AMENDED). The process according to claim 1056, wherein Sig eomprises is a non-radioactively detectable indicator moiety molecule.

Claim 1114 (CURRENTLY AMENDED). The process according to claim 1113, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 1115 (PREVIOUSLY PRESENTED). The process according to claim 1114, wherein said aromatic structure is heterocyclic.

Claim 1116 (PREVIOUSLY PRESENTED). The process according to claim 1115, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1117 (CURRENTLY AMENDED). The process according to claim 1116, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 1118 (CANCELED).

Claim 1119 (CANCELED).

Claim 1120 (CANCELED).

Claim 1121 (CANCELED).

Claim 1122 (CANCELED).

Claim 1123 (CURRENTLY AMENDED). The process according to claim 1098, wherein <u>said A</u> or <u>said</u> Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

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Claim 1124 (CANCELED).

Claim 1125 (CANCELED).

Claim 1126 (CURRENTLY AMENDED). The process according to claim 1113, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and or a combination of any of the foregoing.

Claim 1127 (CANCELED).

Claim 1128 (CANCELED).

Claim 1129 (CANCELED).

Claim 1130 (CANCELED).

Claim 1131 (CANCELED).

Claim 1132 (CANCELED).

Claim 1133 (CANCELED).

Claim 1134 (CANCELED).

Claim 1135 (CANCELED).

Claim 1136 (PREVIOUSLY CANCELED).

Claim 1137 (CANCELED).

Page 75 [Supplemental Amendment To Applicants' December 31, 2003 Amendment – July 13, 2004] Claim 1138 (CANCELED). Claim 1139 (PREVIOUSLY CANCELED). Claim 1140 (CANCELED). Claim 1141 (CANCELED). Claim 1142 (CANCELED). Claim 1143 (CANCELED). Claim 1144 (PREVIOUSLY CANCELED). Claim 1145 (PREVIOUSLY CANCELED). Claim 1146 (CANCELED). Claim 1147 (CANCELED). Claim 1148 (CANCELED). Claim 1149 (CANCELED). Claim 1150 (CANCELED). Claim 1151 (CANCELED). Claim 1152 (CANCELED).

Enz-5(D8)(C2)

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Claim 1153 (CANCELED).

Claim 1154 (CANCELED).

Claim 1155 (CANCELED).

Claim 1156 (CANCELED).

Claim 1157 (CANCELED).

Claim 1158 (CANCELED).

Claim 1159 (CANCELED).

Claim 1160 (CANCELED).

Claim 1161 (CANCELED).

Claim 1162 (CANCELED).

Claim 1163 (CURRENTLY AMENDED). The process according to claim 1025, wherein said detectable labeled nucleic acid fragments are detectable <u>by a non-radioactive means comprising</u> non-radioactively by a fluorescent measurement, a chromogenic measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1164 (PREVIOUSLY PRESENTED). The process according to claim 1025, wherein <u>in</u> said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

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Claim 1165 (CURRENTLY AMENDED). The process according to claims 1025, or 1056 or 1057, wherein said detecting step is carried out directly.

Claim 1166 (CURRENTLY AMENDED). The process according to claim 1165, wherein the detectable non-radioactive labeled fragments comprise one or more non-radioactively detectable indicator moieties molecules and said direct detection is carried out using these indicator moieties molecules.

Claim 1167 (CURRENTLY AMENDED). The process according to claim 1166, wherein said non-radioactively detectable indicator <u>moieties</u> <u>molecules</u> comprise fluorescently labeled nucleotides.

Claim 1168 (PREVIOUSLY PRESENTED). The process according to claim 1167, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1169 (CURRENTLY AMENDED). The process according to claim 1165, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 1170 (CURRENTLY AMENDED). The process according to claim 1165, wherein <u>in</u> said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating structure, a fluorogenic structure, a chromogenic structure, a chemiluminescent structure and <u>or</u> an electron dense structure.

Claim 1171 (PREVIOUSLY CANCELED).

Claim 1172 (CURRENTLY AMENDED). The process according to claims 1025, or 1056 or 1057, wherein said detecting step is carried out by means of an indirectly detectable signal provided

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by said one or more non-radioactive modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 1173 (CURRENTLY AMENDED). The process according to claim 1172, wherein <u>in</u> said detecting step the indirectly detectable signal <u>is selected from the group consisting of</u> an antibody, an antigen, a hapten, a receptor, a ligand <u>and or</u> an enzyme.

Claim 1174 (PREVIOUSLY CANCELED).

Claim 1175 (CURRENTLY AMENDED). The process according to claim 1025, wherein said one or more modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs are capable of being detected by a <u>member selected from the group consisting of</u> an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and <u>or</u> an electron density measurement.

Claim 1176 (CURRENTLY AMENDED). The process according to claim 1025, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs.

Claim 1177 (CURRENTLY AMENDED). A process for determining with a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid of interest or a portion thereof, said process comprising:

# (A) providing

- (1) one or more nucleotides or nucleotide analogs that are: (a) non-radioactive and (b) chemically modified or chemically labeled so as to be detectable provided that said nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid; or
- (2) one or more oligonucleotides or polynucleotides comprising at least one of said nucleotides or nucleotide analogs (1); or

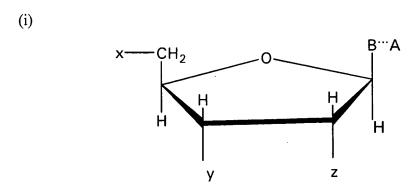
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## (3) both (1) and (2); and

### (B) providing at least one nucleic acid of interest;

wherein said nucleotides or nucleotide analogs (1) and said oligonucleotides and polynucleotides (2) are capable of attaching to, or coupling to, or incorporating into, or forming one or more nucleic acid fragments, and wherein said nucleotides or nucleotide analogs (1) have been non-radioactively modified or non-radioactively labeled, non-disruptively or disruptively, on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof; and;

(BC) incorporating said nucleotides or nucleotide analogs (1) or said oligonucleotides or polynucleotides (2), or both (1) and (2), into or onto one or more of said nucleic acid fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, and wherein said nucleotides or nucleotide analogs (1) comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of comprising one or more of the following:



wherein B represents comprises a purine moiety, a 7-deazapurine moiety, or a pyrimidine moiety, and B is covalently bonded to the C1-position of the furanose furanosyl moiety provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanose furanosyl moiety is attached at the N9 position of the purine moiety or of the 7-deazapurine moiety and whenever B is a pyrimidine moiety, the furanose furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

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wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and wherein x comprises a member selected from the group consisting of:

wherein y comprises a member-selected from the group consisting of:

wherein z comprises a member selected from the group consisting of H-and or HO-;

(ii)

#### wherein

PM is a phosphate moiety,
SM is a furanose furanosyl moiety,
BASE is a base moiety, and

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Sig is a detectable non-radioactive moiety, and or wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

- (CD) transferring or subjecting said detectable non-radioactive labeled fragments to a sequencing gel;
  - $(\underline{\partial E})$  separating or resolving said detectable non-radioactive labeled fragments; and
- $(\underline{E}\underline{F})$  non-radioactively detecting directly or indirectly the presence of said detectable non-radioactive labeled fragments to determine the sequence of said nucleic acid of interest.

Claim 1178 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 1179 (CURRENTLY AMENDED). The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, mammals, and or a combination of any of the foregoing.

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Claim 1180 (CANCELED).

Claim 1181 (CURRENTLY AMENDED). The process according to claim 1180 1179, wherein said mammal comprises a human being mammals comprise human beings.

Claim 1182 (PREVIOUSLY PRESENTED). The process according to claim 1178, wherein said organism is living.

Claim 1183 (CURRENTLY AMENDED). The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 1184 (CANCELED).

Claim 1185 (CURRENTLY AMENDED). The process according to claim 1184 1183, wherein said eukaryotic nucleic acid sequence of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 1186 (CANCELED).

Claim 1187 (CANCELED).

Claim 1188 (CANCELED).

Claim 1189 (CANCELED).

Claim 1190 (CURRENTLY AMENDED). The process according to claim 1189 <u>1185</u>, wherein said human mammalian chromosomal nucleic acid sequence of interest comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

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Claim 1191 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said incorporating step is carried out using an enzyme.

Claim 1192 (PREVIOUSLY PRESENTED). The process according to claim 1191, wherein said enzyme comprises a polymerase.

Claim 1193 (PREVIOUSLY PRESENTED). The process according to claim 1191, wherein said polymerase comprises DNA polymerase.

Claim 1194 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said nucleotides or nucleotide analogs (1) comprise a nucleoside di- or tri-phosphate.

Claim 1195 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said incorporating step is template dependent or template independent.

Claim 1196 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said incorporating step is template dependent.

Claim 1197 (CURRENTLY AMENDED). The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one internal modified nucleotide or internal modified nucleotide analog (1).

Claim 1198 (CURRENTLY AMENDED). The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one terminal modified nucleotide or <u>terminal modified</u> nucleotide analog (1).

Claim 1199 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said nucleotide analog ean be has been attached terminally to DNA or RNA by means of an enzyme.

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Claim 1200 (PREVIOUSLY PRESENTED). The process according to claim 1199, wherein said enzyme comprises terminal transferase.

Claim 1201 (PREVIOUSLY CANCELED).

Claim 1202 (PREVIOUSLY CANCELED).

Claim 1203 (PREVIOUSLY CANCELED).

Claim 1204 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said incorporation comprises nick translation.

Claim 1205 (PREVIOUSLY CANCELED).

Claim 1206 (PREVIOUSLY CANCELED).

Claim 1207 (PREVIOUSLY CANCELED).

Claim 1208 (CURRENTLY AMENDED). The process according to claim 1177, wherein PM is selected from the group consisting of comprises a monophosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

Claim 1209 (CURRENTLY AMENDED). The process according to claim 1177, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) <u>eomprise</u> a nucleoside mono-, di- or tri-phosphate.

Claim 1210 (CANCELED).

Claim 1211. (PREVIOUSLY CANCELED).

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Claim 1212 (CURRENTLY AMENDED). The process according to claim 1177, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2', 3'-dideoxyribose.

Claim 1213 (CURRENTLY AMENDED). The process according to claim 1177, wherein B in said nucleotide structure or nucleotide analog structure (i), and BASE in nucleotide structure or nucleotide analog structure (ii) or (iii), is selected from the group consisting of comprises a pyrimidine moiety, a purine moiety, a 7-deazapurine moiety, and or a combination of any of the foregoing.

Claim 1214 (CURRENTLY AMENDED). The process according to claim 1177, wherein in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i): when B is a purine, A is attached to the 8-position of the purine moiety; when B is a 7-deazapurine moiety, A is attached to the 7-position of the deazapurine moiety; and when B is a pyrimidine moiety, A is attached to the 5-position of the pyrimidine moiety.

Claim 1215 (CURRENTLY AMENDED). The process according to claim 1177, wherein in <u>said</u> nucleotide or nucleotide analog structure (i), A is covalently attached to B at a <u>position when B is a pyrimidine that is selected from the group consisting of the C5 position</u>, the C2 position, the N3 position, the C6 position, and <u>or</u> combinations thereof <u>when B is a pyrimidine</u>, or is covalently attached to B at a <u>position when B is a purine that is selected from the group consisting of the C8 position</u>, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and <u>or combinations thereof</u>, when B is a purine, or is covalently attached to the 7-position when b is a 7-deazapurine.

Claim 1216 (CURRENTLY AMENDED). The process according to claim 1177, wherein in said nucleotide <u>structure</u> or nucleotide analog structure (i) A is covalently attached to B at a position selected from the group consisting of <u>comprising</u> the  $N^4$  position when said pyrimidine comprises cytosine, the  $N^2$  position when said purine comprises adenine or deazaadenine, the  $N^6$  position when said purine comprises guanine or deazaguanine, and <u>or</u> combinations thereof.

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Claim 1217 (PREVIOUSLY CANCELED).

Claim 1218 (CURRENTLY AMENDED). The process according to claim 1177, wherein at in said incorporating step, A in the nucleotide <u>structure</u> or nucleotide analog structure (i) is covalently attached to B through a linkage group.

Claim 1219 (PREVIOUSLY PRESENTED). The process according to claim 1218, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1220 (CURRENTLY AMENDED). The process according to claim 1218, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>eontains</u> <u>comprises</u> an amine.

Claim 1221 (PREVIOUSLY PRESENTED). The process according to claim 1220, wherein said amine comprises a primary amine.

Claim 1222 (CURRENTLY AMENDED). The process according to claim 1177, wherein <u>in</u> said incorporating step, Sig in the nucleotide <u>structure</u> or nucleotide analog structure (ii) is covalently attached to SM through a linkage group.

Claim 1223 (PREVIOUSLY PRESENTED). The process according to claim 1222, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1224 (CURRENTLY AMENDED). The process according to claim 1222, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>contains</u> <u>comprises</u> an amine.

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Claim 1225 (PREVIOUSLY PRESENTED). The process according to claim 1224, wherein said amine comprises a primary amine.

Claim 1226 (CURRENTLY AMENDED). The process according to claim 1177, wherein in said incorporating step, Sig in the nucleotide <u>structure</u> or nucleotide analog structure (iii) is covalently attached to PM through a linkage group.

Claim 1227 (PREVIOUSLY PRESENTED). The process according to claim 1226, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1228 (CURRENTLY AMENDED). The process according to claim 1226, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>eontains</u> <u>comprises</u> an amine.

Claim 1229 (PREVIOUSLY PRESENTED). The process according to claim 1228, wherein said amine comprises a primary amine.

Claim 1230 (CURRENTLY AMENDED). The process according to claim 1211 1177, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1231 (CURRENTLY AMENDED). The process according to claim 1211 1177, wherein in said nucleotide <u>structure</u> or nucleotide analog structure (iii), PM is attached to SM at a <u>position</u> independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a

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pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1232 (CURRENTLY AMENDED). The process according to claim 1177, wherein said covalent attachment in nucleotide <u>structure</u> or nucleotide analog structure (iii) is <u>selected from the group consisting of comprises:</u>

and or

Claim 1233 (CURRENTLY AMENDED). The process according to claim 1177, wherein PM is comprises a mono-, di- or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1234 (CURRENTLY AMENDED). The process according to claim 1177, wherein said covalent attachment in any of nucleotide <u>structure</u> or nucleotide analog structure (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

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1235 (CURRENTLY AMENDED). The process according to claim 1177, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises a member selected from the group consisting of: a —CH<sub>2</sub>NH— moiety, an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide <u>structure</u> or nucleotide analog structure (i), or both.

Claim 1236 (CURRENTLY AMENDED). The process according to claim 1177, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 1237 (CURRENTLY AMENDED). The process according to claim 1177, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises or includes: an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2 - NH_-$$
,
 $-CH = CH - CH_2 - NH_-$ ,
 $-CH = CH - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH = CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 -$ 

Claim 1238 (CURRENTLY AMENDED). The process according to claim 1177, wherein, in <u>said</u> nucleotide or nucleotide analog structure (i), said covalent attachment <u>includes comprises</u> a glycosidic linkage moiety.

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Claim 1239 (CURRENTLY AMENDED). The process according to claim 1177, wherein in said nucleotide <u>structure</u> or nucleotide analog structure (i), A is covalently attached to B through a linkage group, or in said nucleotide <u>structure</u> or nucleotide analog structure (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1240 (CURRENTLY AMENDED). The process according to claim 1239, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said linkage group <u>eontains</u> <u>comprises</u> an amine.

Claim 1241 (PREVIOUSLY PRESENTED). The process according to claim 1240, wherein said amine comprises a primary amine.

Claim 1242 (PREVIOUSLY PRESENTED). The process according to claim 1239, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1243 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said A or Sig comprises at least three carbon atoms.

Claim 1244 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1245 (CANCELED).

Claim 1246 (CANCELED).

Claim 1247 (CANCELED).

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Claim 1248 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said A or Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1249 (CURRENTLY AMENDED). The process according to claim 1177, where said A or Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and, a chelating component or any combination thereof.

Claim 1250 (CANCELED).

Claim 1251 (PREVIOUSLY CANCELED).

Claim 1252 (CANCELED).

Claim 1253 (CURRENTLY AMENDED). The process according to claim 1252 1249, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 1254 (PREVIOUSLY CANCELED).

Claim 1255 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said A or Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 1256 (PREVIOUSLY PRESENTED). The process according to claim 1255, wherein the binding protein comprises a lectin.

Claim 1257 (PREVIOUSLY PRESENTED). The process according to claim 1256, wherein the lectin comprises concanavalin A.

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Claim 1258 (PREVIOUSLY PRESENTED). The process according to claim 1256, wherein said lectin is conjugated to ferritin.

Claim 1259 (PREVIOUSLY CANCELED).

Claim 1260 (PREVIOUSLY CANCELED).

Claim 1261 (CANCELED).

Claim 1262 (CANCELED).

Claim 1263 (CURRENTLY AMENDED). The process according to claim 1262 1249, wherein said metal-containing component is catalytic.

Claim 1264 (CURRENTLY AMENDED). The process according to claim 1177, wherein A or Sig eomprises is a non-radioactively detectable indicator moiety molecule.

Claim 1265 (CURRENTLY AMENDED). The process according to claim 1264, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 1266 (PREVIOUSLY PRESENTED). The process according to claim 1265, wherein said aromatic structure is heterocyclic.

Claim 1267 (PREVIOUSLY PRESENTED). The process according to claim 1266, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1268 (CURRENTLY AMENDED). The process according to claim 1267, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, and dansyl, or any combination thereof.

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Claim 1269 (PREVIOUSLY PRESENTED). The process according to claim 1268, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1270 (CURRENTLY AMENDED). The process according to claim 1264, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and or a combination of any of the foregoing.

Claim 1271 (CANCELED).

Claim 1272 (CURRENTLY AMENDED). The process according to claim 1271 1249, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine, and dansyl or any combination thereof.

Claim 1273 (CANCELED).

Claim 1274 (CANCELED).

Claim 1275 (CURRENTLY AMENDED). The process according to claim 1249, wherein said A or Sig comprises an antigenic or hapten component capable of completing complexing with an antibody specific to the component.

Claim 1276 (CANCELED).

Claim 1277 (CANCELED).

Claim 1278 (CURRENTLY AMENDED). The process according to claim 1177, wherein any of said nucleotide structure or nucleotide analog structure (i), (ii) and (iii) is detectable by a means selected from the group consisting of comprising a fluorescent measurement, and a chemiluminescent measurement, or a combination thereof.

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Claim 1279 (CURRENTLY AMENDED). The process according to claim 1177, wherein <u>said</u> A or Sig is detectable when it is attached to the nucleotide <u>structure</u> or nucleotide analog structure (i), (ii) or (iii) directly or through a linkage group.

Claim 1280 (PREVIOUSLY PRESENTED). The process according to claim 1279, wherein said linkage group does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 1281 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said detectable non-radioactive labeled nucleic acid fragment or fragments are terminally ligated or attached to a polypeptide.

Claim 1282 (CURRENTLY AMENDED). The process according to claim 1281, wherein the <u>said</u> polypeptide comprises a polylysine.

Claim 1283 (CURRENTLY AMENDED). The process according to claim 1281, wherein the said polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1284 (PREVIOUSLY PRESENTED). The process according to claim 1281, wherein said A or Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1285 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said separating step is carried out electrophoretically.

Claim 1286 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said detecting step is carried out directly.

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Claim 1287 (CURRENTLY AMENDED). The process according to claim 1286, wherein said direct detection is carried out on one or more non-radioactively detectable indicator <del>moieties</del> molecules.

Claim 1288 (CURRENTLY AMENDED). The process according to claim 1287, wherein said non-radioactively detectable indicator moieties molecules comprise fluorescently labeled nucleotides.

Claim 1289 (PREVIOUSLY PRESENTED). The process according to claim 1288, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1290 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said detecting step is carried out by means of a directly detectable signal provided by said A or Sig detectable non-radioactive moiety.

Claim 1291 (CURRENTLY AMENDED). The process according to claim 1290, wherein <u>in</u> said detecting step, the directly detectable signal providing A or Sig detectable non-radioactive moiety comprises a <u>member selected from the group consisting of</u> a fluorogenic structure, a chromogenic structure, a chemiluminescent structure <u>and or</u> an electron dense structure.

Claim 1292 (CURRENTLY AMENDED). The process according to claim 1290, wherein <u>in</u> said detecting step the directly detectable signal is provided by an enzyme.

Claim 1293 (PREVIOUSLY PRESENTED). The process according to claim 1177, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said A or Sig detectable non-radioactive moiety.

Claim 1294 (CURRENTLY AMENDED). The process according to claim 1293, wherein <u>in</u> said detecting step, the indirectly detectable signal is provided by a member selected from the group eonsisting of which comprises an antibody, an antigen, a hapten, a receptor, a ligand and <u>or</u> an

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enzyme.

Claim 1295 (PREVIOUSLY CANCELED).

Claim 1296 (PREVIOUSLY PRESENTED). The process according to claim 1293, wherein <u>in</u> said detecting step, the indirectly detectable signal providing Sig comprises a structure capable of binding to an insoluble phase.

Claim 1297 (CURRENTLY AMENDED). The process according to claim 1177, wherein said Sig detectable non-radioactive moiety is capable of being detected by means comprising a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1298 (CURRENTLY AMENDED). A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (a) providing a sample which may contain a nucleic acid of interest;
- (b) \_\_\_\_specifically hybridizing said nucleic acid of interest in the sample with one or more detectable non-radioactive labeled oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of which comprises one or more of:
  - (i) a nucleotide structure or nucleotide analog structure having the formula

wherein

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PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety that comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive <u>non-nucleotidyl</u> moiety that comprises at least three carbon atoms,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

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#### wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive <u>non-nucleotidyl</u> moiety that comprises at least three carbon atoms,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(b) detecting non-radioactively the presence of Sig in any of the detectable non-radioactive labeled oligo- or polynucleotides which have hybridized to said nucleic acid of interest.

Claim 1299 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

Claim 1300 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the nucleic acid of interest is double-stranded or single-stranded.

Claim 1301 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the nucleic acid of interest has been rendered single-stranded.

Claim 1302 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the nucleic acid of interest is derived from an organism.

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Claim 1303 (CURRENTLY AMENDED). The process according to claim 1302, wherein the organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 1304 (CURRENTLY AMENDED). The process according to elaims claim 1302 or 1305, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 1305 (PREVIOUSLY PRESENTED). The process according to claim 1302, wherein said organism is living.

Claim 1306 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

Claim 1307 (CURRENTLY AMENDED). The process according to claim 1306, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of comprises bacteria, virus and or fungi.

Claim 1308 (CURRENTLY AMENDED). The process according to claim 1298, wherein said nucleic acid of interest is derived from an organism a member selected from the group consisting of which comprises Streptococcus pyrogenes, Neisseria meningitidis, Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Neisseria gonorrhoeae, Mycobacterium tuberculosis, and or any combinations of the foregoing.

Claim 1309 (CURRENTLY AMENDED). The process according to claim 1298, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae* sequences.

Claim 1310 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts

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resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

Claim 1311 (CURRENTLY AMENDED). The process according to claim 1310, wherein when said bacterium is comprises Steptococcus pyrogenes or Neisseria meningtidis, said antibiotic is comprises penicillin, wherein when said bacterium is comprises Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Streptococcus pyrogenes, or Neisseria gonorrhoeae, said antibiotic is comprises a tetracycline, and wherein when said bacterium is comprises

Mycobacterium tuberculosis, said antibiotic is comprises an aminoglycoside.

Claim 1312 (CURRENTLY AMENDED). The process according to claim 1311, wherein said bacterium is <u>comprises</u> *Neisseria gonorrhoeae* and said antibiotic is <u>selected from the group</u> eonsisting of <u>comprises</u> penicillin, tetracycline, aminoglycoside and <u>or</u> combinations thereof.

Claim 1313 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

Claim 1314 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

Claim 1315 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides which are complementary to a series of known genetic sequences located on chromosomes.

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Claim 1316 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid which includes a terminal polynucleotide sequence poly A and wherein the oligo- or polynucleotide comprises a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition of Sig to the 5' position of said uracil moiety.

Claim 1317 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

Claim 1318 (CURRENTLY AMENDED). The process according to claim 1298, wherein said nucleotide <u>structure</u> or nucleotide analog structure (i), (ii) or (iii) <u>ean be has been</u> attached terminally to DNA or RNA by means of an enzyme.

Claim 1319 (PREVIOUSLY PRESENTED). The process according to claim 1318, wherein said enzyme comprises terminal transferase.

Claim 1320 (CURRENTLY AMENDED). The process according to claim 1298, wherein said nucleotide <u>structure</u> or nucleotide analog structure (i), (ii) or (iii) <u>ean be has been coupled to DNA</u> or RNA by a coupling means <u>selected from the group consisting of comprising</u> chemical coupling <u>and or enzymatic coupling</u>.

Claim 1321 (CURRENTLY AMENDED). The process according to claim 1320, wherein said chemical coupling ean be has been carried out by a chemical coupling means selected from the group consisting of comprising carbodiimide and or formaldehyde.

Claim 1322 (CURRENTLY AMENDED). The process according to claim 1320, wherein said enzymatic coupling ean be has been carried out by an enzymatic coupling means selected from the group consisting of comprising DNA ligase and or RNA ligase.

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Claim 1323 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said incorporation comprises nick translation.

Claim 1324 (PREVIOUSLY PRESENTED). The process according to claim 1298 or 1323, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1325 (PREVIOUSLY PRESENTED). The process according to claim 1324, wherein said polymerizing enzyme comprises a polymerase.

Claim 1326 (CURRENTLY AMENDED). The process according to claim 1325, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 1327 (CURRENTLY AMENDED). The process according to claim 1298, wherein PM is selected from the group consisting of comprises a monophosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

Claim 1328 (CURRENTLY AMENDED). The process according to claim 1298, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 1329 (CANCELED).

Claim 1330. (PREVIOUSLY CANCELED).

Claim 1331 (CURRENTLY AMENDED). The process according to claim 1329 1298, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2',3'-dideoxyribose.

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Claim 1332 (CURRENTLY AMENDED). The process according to claim 1298, wherein BASE in any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) is <u>comprises</u> a 7-deazapurine.

Claim 1333 (PREVIOUSLY CANCELED).

Claim 1334 (CURRENTLY AMENDED). The process according to claim 1298, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise nucleotide or nucleotide analog structure (i) and Sig in said nucleotide or nucleotide analog structure (i) is covalently attached to BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and or combinations thereof when BASE is a pyrimidine, and said Sig is covalently attached to the BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when BASE is a purine, or as covalently attached to the 7 position when BASE is a 7'-deazapurine.

Claim 1335 (CURRENTLY AMENDED). The process according to claim 1298, wherein said Sig in said nucleotide structure or nucleotide analog structure (i) is covalently attached to said BASE at a position selected from the group consisting of comprising the  $N^4$  position when said pyrimidine comprises cytosine, the  $N^2$  position when said purine comprises adenine or deazaadenine, the  $N^6$  position when said purine comprises guanine or deazaguanine, and or combinations thereof.

Claim 1336 (CURRENTLY AMENDED). The process according to claim 13331298, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

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Claim 1337 (CURRENTLY AMENDED). The process according to claim 13331298, wherein in said nucleotide structure or nucleotide analog structure (iii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1338 (CURRENTLY AMENDED). The process according to claim 1298, wherein said covalent attachment in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (iii) <u>is selected from the group consisting of comprises:</u>

and or

Claim 1339 (CURRENTLY AMENDED). The process according to claim 1298, wherein PM is comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Ο.

Claim 1340 (CURRENTLY AMENDED). The process according to claim 1298, wherein said covalent attachment in any of nucleotide structure or nucleotide analog structure (i), (ii) or (iii) does

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not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claim 1341 (CURRENTLY AMENDED). The process according to claim 1298, wherein, in nucleotide or nucleotide analog structure (i), said covalent attachment comprises a member selected from the group consisting of: a — $CH_2NH$ — moiety, an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i) or both.

Claim 1342 (CURRENTLY AMENDED). The process according to claim 1298, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 1343 (CURRENTLY AMENDED). The process according to claim 1298, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises or includes: an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or any of the moieties

Claim 1344 (CURRENTLY AMENDED). The process according to claim 1298, wherein, in nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment <u>includes</u> <u>comprises</u> a glycosidic linkage moiety.

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Claim 1345 (CURRENTLY AMENDED). The process according to claim 1298, wherein in any of said nucleotide <u>structure</u> or nucleotide analog structure (i), (ii) or (iii), said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1346 (CURRENTLY AMENDED). The process according to claim 1345, wherein, in nucleotide <u>structures</u> or nucleotide analog structures (i), said linkage group <u>contains</u> comprises an amine.

Claim 1347 (PREVIOUSLY PRESENTED). The process according to claim 1346, wherein said amine comprises a primary amine.

Claim 1348 (PREVIOUSLY PRESENTED). The process according to claim 1345, wherein said linkage group does not substantially interfere with nucleic acid hybridization or double-stranded nucleic acid formation.

Claim 1349 (PREVIOUSLY PRESENTED). The process according to claim 1345, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1350 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein Sig comprises at least three carbon atoms.

Claim 1351 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1352 (CANCELED).

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Claim 1353 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1354 (PREVIOUSLY PRESENTED). The process according to claim 1353, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1355 (CANCELED).

Claim 1356 (CANCELED).

Claim 1357 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1358 (CURRENTLY AMENDED). The process according to claim 1298, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component or any combination of the foregoing.

Claim 1359 (CANCELED).

Claim 1360 (CURRENTLY AMENDED). The process according to claim 1359 1358, wherein said electron dense component comprises ferritin.

Claim 1361 (CANCELED).

Claim 1362 (CURRENTLY AMENDED). The process according to claim 1361 1358, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

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Claim 1363 (CURRENTLY AMENDED). The process according to claim 1361 1358, wherein said magnetic component comprises magnetic beads.

Claim 1364 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

Claim 1365 (PREVIOUSLY PRESENTED). The process according to claim 1364, wherein the binding protein comprises a lectin.

Claim 1366 (PREVIOUSLY PRESENTED). The process according to claim 1365, wherein the lectin comprises concanavalin A.

Claim 1367 (PREVIOUSLY PRESENTED). The process according to claim 1365, wherein said lectin is conjugated to ferritin.

Claim 1368 (PREVIOUSLY PRESENTED). The process according to claim 1358, wherein Sig comprises an enzyme.

Claim 1369 (CURRENTLY AMENDED). The process according to claim 1368, wherein said enzyme is selected from the group consisting of comprises alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase, and peroxidase, or a combination thereof.

Claim 1370 (CANCELED).

Claim 1371 (CANCELED).

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Claim 1372 (CURRENTLY AMENDED). The process according to claim 1371 1358, wherein said metal-containing component is catalytic.

Claim 1373 (CURRENTLY AMENDED). The process according to claim 1298, wherein Sig eomprises is a non-radioactively detectable indicator moiety molecule.

Claim 1374 (CURRENTLY AMENDED). The process according to claim 1373, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 1375 (PREVIOUSLY PRESENTED). The process according to claim 1374, wherein said aromatic structure is heterocyclic.

Claim 1376 (PREVIOUSLY PRESENTED). The process according to claim 1375, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1377 (CURRENTLY AMENDED). The process according to claim 1376, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 1378 (PREVIOUSLY PRESENTED). The process according to claim 1377, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1379 (PREVIOUSLY PRESENTED). The process according to claim 1358, wherein Sig comprises a fluorescent component.

Claim 1380 (CURRENTLY AMENDED). The process according to claim 1379, wherein said fluorescent component is selected from the group consisting of comprises fluorescein, rhodamine and, dansyl, or any combination of any of the foregoing.

Claim 1381 (CANCELED).

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Claim 1382 (CANCELED).

Claim 1383 (CURRENTLY AMENDED). The process according to claim 1358, wherein <u>said</u> Sig comprises an antigenic or hapten component <u>is</u> capable of complexing with an antibody specific to the component.

Claim 1384 (CANCELED).

Claim 1385 (CANCELED).

Claim 1386 (CURRENTLY AMENDED). The process according to claim 1373, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and or a combination of any of the foregoing.

Claim 1387 (CURRENTLY AMENDED). The process according to claim 1298, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) and (iii) are detectable by a means selected from the group consisting of comprising a fluorescent measurement, and a chemiluminescent measurement, or a combination thereof.

Claim 1388 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

Claim 1389 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group.

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Claim 1390 (PREVIOUSLY PRESENTED). The process according to claim 1389, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claim 1391 (CURRENTLY AMENDED). The process according to claim 1298, wherein Sig in said nucleotide <u>structure</u> or nucleotide analog structure (iii) is covalently attached to PM via the chemical linkage

Claim 1392 (CANCELED).

Claim 1393 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

Claim 1394 (PREVIOUSLY PRESENTED). The process according to claim 1298, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

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Claim 1395 (CURRENTLY AMENDED). The process according to claims 1393 or 1394, wherein the <u>said</u> polypeptide comprises a polylysine.

Claim 1396 (CURRENTLY AMENDED). The process according to claims 1393 or 1394, wherein the <u>said</u> polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1397 (PREVIOUSLY PRESENTED). The process according to claim 1394, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1398 (CURRENTLY AMENDED). The process according to claim 1394, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component or any combination of any of the foregoing.

Claim 1399 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said detecting step is carried out directly.

Claim 1400 (CURRENTLY AMENDED). The process according to claim 1399, wherein said direct detection is carried out by non-radioactively detecting indicator moieties molecules on the modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1401 (CURRENTLY AMENDED). The process according to claim 1400, wherein said indicator moieties molecules comprise fluorescently labeled nucleotides.

Claim 1402 (PREVIOUSLY PRESENTED). The process according to claim 1401, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

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Claim 1403 (PREVIOUSLY PRESENTED). The process according to claim 1298, wherein said detecting step is carried out by means of a directly detectable non-radioactive signal provided by Sig.

Claim 1404 (CURRENTLY AMENDED). The process according to claim 1403, wherein <u>in</u> said detecting step, the directly detectable non-radioactive signal comprises a <u>member selected from the group consisting of</u> a fluorogenic structure, a phosphorescent structure, a chromogenic structure, a chemiluminescent structure and <u>or</u> an electron dense structure.

Claim 1405 (CURRENTLY AMENDED). The process according to claim 1403, wherein <u>in</u> said detecting step, the directly detectable non-radioactive signal is provided by an enzyme.

Claim 1406 (CURRENTLY AMENDED). The process according to claim 1298, wherein said detecting step is carried out by means of an indirectly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety.

Claim 1407 (CURRENTLY AMENDED). The process according to claim 1406, wherein <u>in</u> said detecting step, the indirectly detectable non-radioactive signal <u>is selected from the group consisting</u> of <u>comprises</u> an antibody, an antigen, a hapten, a receptor, a ligand <u>and or</u> an enzyme.

Claim 1408 (PREVIOUSLY CANCELED).

Claim 1409 (CURRENTLY AMENDED). The process according to claim 1298, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group eonsisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1410 (CURRENTLY AMENDED). The process according to claim 12551298, further comprising one or more washing steps.

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Claim 1411 (CURRENTLY AMENDED). A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (A) providing a sample which may contain a nucleic acid of interest;
- (B) providing:
- (i) an oligo- or polynucleotide that comprises two segments, the first segment comprising a nucleotide sequence that is complementary to and capable of specifically hybridizing to and forming a hybrid with a <u>said</u> nucleic acid of interest or a portion thereof, and the second segment comprising an operator sequence that is capable of binding to or complexing with a non-radioactively detectable protein; and
- (ii) a non-radioactively detectable protein which is non-radioactive and has a binding affinity to said operator sequence;
- (<u>BC</u>) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said non-radioactively detectable protein (ii) to form a complex; and
- $(\underline{CD})$  detecting non-radioactively the presence of said non-radioactively detectable protein in said complex to detect said nucleic acid of interest.

Claim 1412 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

Claim 1413 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the nucleic acid of interest is double-stranded or single-stranded.

Claim 1414 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the nucleic acid of interest has been rendered single-stranded.

Claim 1415 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the nucleic acid of interest is derived from an organism.

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Claim 1416 (CURRENTLY AMENDED). The process according to claim 1415, wherein the living organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 1417 (CURRENTLY AMENDED). The process according to elaims claim 1415 or 1418, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 1418 (PREVIOUSLY PRESENTED). The process according to claim 1415, wherein said organism is living.

Claim 1419 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

Claim 1420 (CURRENTLY AMENDED). The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of comprises bacteria, virus and or fungi.

Claim 1421 (CURRENTLY AMENDED). The process according to claim 1411, wherein said nucleic acid of interest are <u>is</u> derived from <u>an organism</u> a member selected from the group eonsisting of comprising Streptococcus pyrogenes, Neisseria meningitides, Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Neisseria gonorrhoeae, <u>or</u> Mycobacterium tuberculosis, and any combinations of the foregoing.

Claim 1422 (CURRENTLY AMENDED). The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae sequences*.

Claim 1423 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts

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resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

Claim 1424 (PREVIOUSLY PRESENTED). The process according to claim 1423, wherein when said bacterium is *Steptococcus pyrogenes* or *Neisseria meningtidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside.

Claim 1425 (CURRENTLY AMENDED). The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of comprises penicillin, tetracycline, aminoglycoside and or combinations thereof.

Claim 1426 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

Claim 1427 (CURRENTLY AMENDED). The process according to claim 1411, wherein the <u>said</u> sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

Claim 1428 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes.

Claim 1429 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

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Claim 1430 (CURRENTLY AMENDED). The process according to claim 1411, wherein said non-radioactive detectable protein is selected from the group consisting of comprises an antibody, a promoter, a repressor and or an inducer.

Claim 1431 (PREVIOUSLY PRESENTED). The process according to claim 1430, wherein said repressor comprises a lac repressor.

Claim 1432 (CURRENTLY AMENDED). The process according to claim 1430, wherein said operator at least one protein binding nucleic acid sequence is covalently attached to said oligo- or polynucleotide.

Claim 1433 (CURRENTLY AMENDED). The process according to claim 1432, wherein said covalent attachment <u>has been carried out by comprises</u> ligation.

Claim 1434 (PREVIOUSLY PRESENTED). The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to bind to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Claim 1435 (PREVIOUSLY PRESENTED). The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to be detected non-radioactively when bound to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Claim 1436 (CURRENTLY AMENDED). The process according to claim 1432, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises a <u>member</u> selected from the group consisting of an olefinic bond at the α-position relative to the point of

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attachment to  $\underline{\text{said}}$  nucleotide  $\underline{\text{structure}}$  or nucleotide analog structure (i) , a CH2NH— moiety, or both.

Claim 1437 (CURRENTLY AMENDED). The process according to claim 1436, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 1438 (CURRENTLY AMENDED). The process according to claim 1436, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2 - NH_-,$$
 $-CH = CH - CH_2 - NH_-,$ 
 $-CH = CH - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH = CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 -$ 

Claim 1439 (CURRENTLY AMENDED). The process according to claim 1432, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment <u>includes</u> <u>comprises</u> a glycosidic linkage moiety.

Claim 1440 (CURRENTLY AMENDED). The process according to claim 1432, wherein said operator protein binding sequence is covalently attached to any of the base, phosphate, or furanose furanosyl moieties in said oligo- or polynucleotide.

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Claim 1441 (CURRENTLY AMENDED). The process according to claim 1440, wherein, in <u>said</u> nucleotide <u>structure</u> or nucleotide analog structure (i), said covalent attachment is through a linkage group.

Claim 1442 (CURRENTLY AMENDED). The process according to claim 1441, wherein, in <u>said</u> nucleotide or nucleotide analog structure (i), said linkage group <del>contains</del> comprises an amine.

Claim 1443 (PREVIOUSLY PRESENTED). The process according to claim 1442, wherein said amine comprises a primary amine.

Claim 1444 (CURRENTLY AMENDED). The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said protein binding operator sequence.

Claim 1445 (CURRENTLY AMENDED). The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signalling component or indicator moiety molecule.

Claim 1446 (CURRENTLY AMENDED). The process according to claim 1445, wherein <u>said</u> signalling component or indicator <u>moiety</u> <u>molecule</u> comprises at least three carbon atoms.

Claim 1447 (CURRENTLY AMENDED). The process according to claim 1446, wherein Signalling said signalling component or indicator moiety molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1448 (CURRENTLY AMENDED). The process according to claim 1446, wherein Signalling said signalling component or indicator moiety molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms.

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Claim 1449 (CURRENTLY AMENDED). The process according to claim 1446, wherein Signalling said signalling component or indicator moiety molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1450 (PREVIOUSLY PRESENTED). The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1451 (CURRENTLY AMENDED). The process according to claim 1446, wherein Signalling said signalling component or indicator moiety molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1452 (PREVIOUSLY PRESENTED). The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1453 (CURRENTLY AMENDED). The process according to claim 1446, wherein Signalling said signalling component or indicator moiety molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1454 (CURRENTLY AMENDED). The process according to claim 1445, wherein Signalling said signalling component or indicator moiety molecule comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component, or any combination of any of the foregoing.

Claim 1455 (CURRENTLY AMENDED). The process according to claim 1445, wherein Signalling said signalling component or indicator moiety molecule comprises an aromatic structure.

Claim 1456 (PREVIOUSLY PRESENTED). The process according to claim 1455, wherein said aromatic structure is heterocyclic.

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Claim 1457 (PREVIOUSLY PRESENTED). The process according to claim 1456, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1458 (CURRENTLY AMENDED). The process according to claim 1457, wherein said fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, and dansyl or any combination of any of the foregoing.

Claim 1459 (PREVIOUSLY PRESENTED). The process according to claim 1458, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1460 (CURRENTLY AMENDED). The process according to claim 1454, wherein Signalling said signalling component or indicator moiety molecule comprises a chemiluminescent component.

Claim 1461 (CURRENTLY AMENDED). The process according to claim 1454, wherein Signalling said signalling component or indicator moiety molecule comprises a chelating component.

Claim 1462 (CURRENTLY AMENDED). The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a means selected from the group consisting of a fluorescent measurement, and a chemiluminescent measurement, or a combination thereof.

Claim 1463 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest.

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Claim 1464 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide directly or through a linkage group.

Claim 1465 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said oligo- or polynucleotide is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein.

Claim 1466 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said detecting step is carried out directly.

Claim 1467 (CURRENTLY AMENDED). The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signalling components or indicator moieties molecules.

Claim 1468 (CURRENTLY AMENDED). The process according to claims 1467, wherein said direct detection step is carried out by a member selected from the group consisting of a fluorogenic structure, a chromogenic structure, a chemiluminescent structure, an enzyme, and or an electron dense structure.

Claim 1469 (PREVIOUSLY PRESENTED). The process according to claim 1411, wherein said detecting step is carried out indirectly.

Claim 1470 (CURRENTLY AMENDED). The process according to claim 1469, wherein said indirect detection is carried out by a means selected from the group consisting of comprising an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a structure capable of binding to an insoluble phase, and or a combination of any of the foregoing.

Claim 1471 (CURRENTLY AMENDED). The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by means comprising a member

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selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1472 (PREVIOUSLY PRESENTED). The process according to claim 1411, further comprising one or more washing steps.

Claim 1473 (CURRENTLY AMENDED). A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising:

## providing at least one cell;

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are selected from the group consisting of comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety; and

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Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Enz-5(D8)(C2)

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Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1474 (CURRENTLY AMENDED). A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising:

## providing at least one cell;

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are selected from the group consisting of one or more of comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,
SM is a furanose furanosyl moiety,
BASE is a base moiety, and
Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides,

permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting non-radioactively any of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

Claim 1475 (CURRENTLY AMENDED). A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising:

providing at least one cell;

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providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein said clones or fragments or said oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator moiety and each of said clones or DNA fragments or oligo- or polynucleotides comprises one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are selected from the group consisting of one or more of comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

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detecting non-radioactively any of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

Claim 1476 (CURRENTLY AMENDED). A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

## providing at least one interphase cell;

providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones, wherein said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest and each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are selected from the group consisting of comprise one or more of:

(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

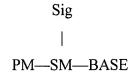
Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a

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position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

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contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and

permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and

comparing each generated signal with other generated signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Claim 1477 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog ean be has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1478 (PREVIOUSLY PRESENTED). The process according to claim 1477, wherein said enzyme comprises terminal transferase.

Claim 1479 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog ean be has been coupled to DNA or RNA by a coupling means selected from the group consisting of comprising chemical coupling and or enzymatic coupling.

Claim 1480 (CURRENTLY AMENDED). The process according to claim 1479, wherein said chemical coupling ean be has been carried out by a chemical coupling means selected from the group consisting of comprising carbodiimide and or formaldehyde.

Claim 1481 (CURRENTLY AMENDED). The process according to claim 1479, wherein said enzymatic coupling can be has been carried out by an enzymatic coupling means selected from the group consisting of comprising DNA ligase and or RNA ligase.

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Claim 1482 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation.

Claim 1483 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1484 (PREVIOUSLY PRESENTED). The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase.

Claim 1485 (CURRENTLY AMENDED). The process according to claim 1484, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 1486 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM is selected from the group consisting of comprises a mono-phosphate, a di-phosphate, a tri-phosphate and or a tetraphosphate.

Claim 1487 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises nucleoside mono-, di- or tri-phosphate.

Claim 1488 (CANCELED).

Claim 1489. (PREVIOUSLY CANCELED).

Claim 1490 (CURRENTLY AMENDED). The process according to claim 1473, 1474, 1475 or 1476, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'-deoxyribose and or 2', 3'-dideoxyribose.

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Claim 1491 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein BASE in any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) is <u>comprises</u> a 7-deazapurine.

Claim 1492 (PREVIOUSLY CANCELED).

Claim 1493 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide <u>structure</u> or nucleotide analog structure (i) is covalently attached to BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and or combinations thereof when BASE is a pyrimidine, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and or combinations thereof when BASE is a purine.

Claim 1494 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide <u>structure</u> or nucleotide analog structure (i) is covalently attached to BASE at a position <u>selected from the group consisting of comprising</u> the N<sup>4</sup> position when said pyrimidine comprises cytosine, the N<sup>2</sup> position when said purine comprises adenine or deazaadenine, the N<sup>6</sup> position when said purine comprises guanine or deazaguanine, and <u>or</u> combinations thereof.

Claim 1495 (CURRENTLY AMENDED). The process according to claim 1489 1473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

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Claim 1496 (CURRENTLY AMENDED). The process according to claim 14891473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (iii), PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1497 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog structure (iii) is selected from the group consisting of comprises

Claim 1498 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM is comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

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Claim 1499 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claim 1500 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a <u>member selected from the group consisting of</u> an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a —CH<sub>2</sub>NH—moiety, or both.

Claim 1501 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises an allylamine group.

Claim 1502 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2 - NH_-$$
,
 $-CH = CH - CH_2 - NH_-$ ,
 $-CH = CH - CH_2 - O - CH_2 - CH_- NH_-$ ,
 $-CH = CH_2 - O - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2$ ,
 $-CH_2 - CH_$ 

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Claim 1503 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of <u>said</u> nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) <u>includes comprises</u> a glycosidic linkage moiety.

Claim 1504 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1505 (CURRENTLY AMENDED). The process according to claim 1504, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group contains an amine.

Claim 1506 (PREVIOUSLY PRESENTED). The process according to claim 1505, wherein said amine comprises a primary amine.

Claim 1507 (PREVIOUSLY PRESENTED). The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1508 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms.

Claim 1509 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1510 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

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Claim 1511 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1512 (PREVIOUSLY PRESENTED). The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1513 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1514 (PREVIOUSLY PRESENTED). The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1515 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1516 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component, or any combination of any of the foregoing.

Claim 1517 (CANCELED).

Claim 1518 (PREVIOUSLY PRESENTED). The process according to claim 1516, wherein said electron dense component comprises ferritin.

Claim 1519 (CANCELED).

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Claim 1520 (CURRENTLY AMENDED). The process according to claim 1519 1516, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 1521 (CURRENTLY AMENDED). The process according to claim 1519 1516, wherein said magnetic component comprises magnetic beads.

Claim 1522 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is empleted complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

Claim 1523 (PREVIOUSLY PRESENTED). The process according to claim 1522, wherein the binding protein comprises a lectin.

Claim 1524 (PREVIOUSLY PRESENTED). The process according to claim 1523, wherein the lectin comprises concanavalin A.

Claim 1525 (PREVIOUSLY PRESENTED). The process according to claim 1523, wherein said lectin is conjugated to ferritin.

Claim 1526 (CANCELED).

Claim 1527 (CURRENTLY AMENDED). The process according to claim 1526 1516, wherein said enzyme is selected from the group consisting of comprises alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

Claim 1528 (CANCELED).

Claim 1529 (CANCELED).

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Claim 1530 (CURRENTLY AMENDED). The process according to claim <del>1529</del>1516, wherein said metal-containing component is catalytic.

Claim 1531 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig emprises is a non-radioactively detectable indicator moiety molecule.

Claim 1532 (CURRENTLY AMENDED). The process according to claim 1531, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 1533 (PREVIOUSLY PRESENTED). The process according to claim 1532, wherein said aromatic structure is heterocyclic.

Claim 1534 (PREVIOUSLY PRESENTED). The process according to claim 1533, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1535 (CURRENTLY AMENDED). The process according to claim 1534, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, dansyl, and or a combination of any of the foregoing.

Claim 1536 (PREVIOUSLY PRESENTED). The process according to claim 1535, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1537 (PREVIOUSLY PRESENTED). The process according to claim 1516, wherein Sig comprises a fluorescent component.

Claim 1538 (CURRENTLY AMENDED). The process according to claim 15371516, wherein said fluorescent component is selected from the group consisting of comprises fluorescein, rhodamine and or dansyl.

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Claim 1539 (PREVIOUSLY PRESENTED). The process according to claim 1538, wherein said fluorescent component comprises fluorescein.

Claim 1540 (CANCELED).

Claim 1541 (PREVIOUSLY PRESENTED). The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

Claim 1542 (CANCELED).

Claim 1543 (CANCELED).

Claim 1544 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein <u>said</u> Sig detectable non-radioactive moiety <u>eomprises</u> is a non-radioactively detectable indicator <u>moiety molecule</u>.

Claim 1545 (CURRENTLY AMENDED). The process according to claim 1544, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and or a combination of any of the foregoing.

Claim 1546 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of <u>said</u> nucleotide <u>structures</u> or nucleotide analogs <u>structures</u> (i), (ii) and (iii) are detectable by a means <u>selected from the group consisting of comprising</u> a fluorescent measurement, and a chemiluminescent measurement, or a combination thereof.

Claim 1547 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

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Claim 1548 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474,1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group.

Claim 1549 (PREVIOUSLY PRESENTED). The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Claim 1550 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide <u>structure</u> or nucleotide analog structure (iii) is covalently attached to PM via the chemical linkage

Claim 1551 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide <u>structure</u> or nucleotide analog structure (iii) is covalently attached to PM via the <u>a</u> chemical linkage.

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Claim 1552 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo-or polynucleotide is terminally ligated or attached to a polypeptide.

Claim 1553 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

Claim 1554 (PREVIOUSLY PRESENTED). The process according to claim 1552, wherein the polypeptide comprises a polylysine.

Claim 1555 (PREVIOUSLY PRESENTED). The process according to claim 1553, wherein the polypeptide comprises a polylysine.

Claim 1556 (CURRENTLY AMENDED). The process according to claim 1552, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1557 (CURRENTLY AMENDED). The process according to claim 1553, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1558 (PREVIOUSLY PRESENTED). The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1559 (CURRENTLY AMENDED). The process according to claim 1553, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component, or any combination of any of the foregoing.

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Claim 1560 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly.

Claim 1561 (CURRENTLY AMENDED). The process according to claim 1560, wherein said direct detection is carried out on one or more non-radioactively detectable indicator moieties molecules.

Claim 1562 (CURRENTLY AMENDED). The process according to claim 1561, wherein said non-radioactively detectable indicator <u>moieties</u> <u>molecules</u> comprise fluorescently labeled nucleotides.

Claim 1563 (PREVIOUSLY PRESENTED). The process according to claim 1562, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1564 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety.

Claim 1565 (CURRENTLY AMENDED). The process according to claim 1564, wherein said detecting step is carried out by means of a member selected from the group consisting of a fluorogenic structure, a chromogenic structure, a cherniluminescent structure and or an electron dense structure.

Claim 1566 (PREVIOUSLY PRESENTED). The process according to claim 1564, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

Claim 1567 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said Sig detectable non-radioactive moiety.

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Claim 1568 (CURRENTLY AMENDED). The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and or an enzyme.

Claim 1569 (PREVIOUSLY CANCELED).

Claim 1570 (CURRENTLY AMENDED). The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1571 (PREVIOUSLY PRESENTED). The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps.

Claim 1572 (PREVIOUSLY PRESENTED). The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

Claim 1573 (CURRENTLY AMENDED). The process according to claim 1475, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator moiety molecule.

Claim 1574 (PREVIOUSLY PRESENTED). The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means selected from the group consisting of comprising manual means and or automatic means.

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Claim 1575 (PREVIOUSLY PRESENTED). The process according to claim 1574, wherein said manual means comprises visualization.

Claim 1576 (PREVIOUSLY PRESENTED). The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping.

Claim 1577 (CURRENTLY AMENDED). The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator moiety molecule.

Claim 1578 (CURRENTLY AMENDED). The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator moiety molecule.

Claim 1579 (CURRENTLY AMENDED). The process according to claim 1476, wherein said detecting and determining step is carried out by a means selected from the group consisting of comprising manual means and or automatic means.

Claim 1580 (PREVIOUSLY PRESENTED). The process according to claim 1579, wherein said manual means comprises visualization.

Claim 1581 (PREVIOUSLY PRESENTED). The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping.

Claim 1582 (CURRENTLY AMENDED). A process for preparing a detectable non-radioactively labeled oligo- or polynucleotide of interest, comprising:

## (A) providing either:

(1) one or more detectable non-radioactive chemically modified or labeled nucleotides or detectable non-radioactive chemically modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into

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DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of comprising nucleotides, oligonucleotides, and polynucleotides or combinations thereof, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said chemically modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more signalling moieties which are capable of providing directly or indirectly a detectable non-radioactive signal; or

(2) an oligo- or polynucleotide of interest comprising one or more said chemically modified or labeled nucleotides or modified or labeled nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of comprising nucleotides, oligonucleotides and or polynucleotides;

wherein said chemically modified or labeled nucleotides or <u>chemically modified or labeled</u> nucleotide analogs of (1) and (2) have been modified or labeled on at least one of the <del>furanose</del> <u>furanosyl</u> moiety, the phosphate moiety, or the base moiety and comprise a nucleotide structure or nucleotide analog structure <u>selected from the group consisting of one or more of comprising</u>:

(i)

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive <u>non-nucleotidyl</u> moiety that comprises at least three carbon atoms, and

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wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii)

Sig | PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive  $\underline{\text{non-nucleotidyl}}$  moiety that comprises at least three carbon atoms, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii)

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive <u>non-nucleotidyl</u> signalling moiety that comprises at least three carbon atoms and is detected non-radioactively by an enzymatic measurement, a fluorescent

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measurement, a chemiluminescent measurement, an electron density measurement, a magnetic measurement, or any combination of the foregoing measurements; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group; provided that when said nucleotide structure or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

said oligo- or polynucleotide of interest; and

(B) either incorporating said chemically modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a non-radioactive labeled oligo- or polynucleotide of interest, or preparing incorporating or attaching chemically modified or labeled nucleotides or nucleotide analogs or unmodified nucleotides or nucleotide analogs to said oligo- or polynucleotide provided in of interest from said incorporate or attach step (A)(2) above, thereby preparing a non-radioactive labeled oligo- or polynucleotide of interest.

Claim 1583 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said oligo- or polynucleotide of interest is derived from an organism.

Claim 1584 (PREVIOUSLY PRESENTED). The process according to claim 1583, wherein said organism is living.

Claim 1585 (CURRENTLY AMENDED). The process according to claims 1583 or 1584, wherein the organism is selected from the group consisting of comprises prokaryotes and or eukaryotes.

Claim 1586 (CANCELED).

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Claim 1587 (CURRENTLY AMENDED). The process according to claim 1586, wherein said eukaryotic oligo- or polynucleotide of interest is comprises a mammalian nucleic acid sequence contained within a chromosome.

Claim 1588 (CANCELED).

Claim 1589 (CANCELED).

Claim 1590 (CANCELED).

Claim 1591 (CANCELED).

Claim 1592 (CURRENTLY AMENDED). The process according to claim 15911587, wherein said human mammalian chromosomal oligo- or polynucleotide of interest nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 1593 (CURRENTLY AMENDED). The process according to claims 1583 or 1584, wherein said organism is selected from the group consisting of comprises bacteria, fungi, viruses, yeast, or mammals, and a combination of any of the foregoing.

Claim 1594 (CURRENTLY AMENDED). The process according to claim 1584 1593, wherein said living organism comprises a mammal.

Claim 1595 (PREVIOUSLY PRESENTED). The process according to claim 1594, wherein said mammal comprises a human being.

Claim 1596 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said incorporating step is carried out using an enzyme.

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Claim 1597 (PREVIOUSLY PRESENTED). The process according to claim 1596, wherein said enzyme comprises a polymerase.

Claim 1598 (PREVIOUSLY PRESENTED). The process according to claim 1597, wherein said polymerase comprises DNA polymerase.

Claim 1599 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said nucleotide analog can be attached terminally to DNA or RNA by an enzyme.

Claim 1600 (PREVIOUSLY PRESENTED). The process according to claim 1599, wherein said enzyme comprises terminal transferase.

Claim 1601 (CURRENTLY AMENDED). The process according to claim 1582, wherein said nucleotide analog ean be has been coupled to DNA or RNA by a coupling means selected from the group consisting of comprising chemical coupling and or enzymatic coupling.

Claim 1602 (CURRENTLY AMENDED). The process according to claim 1601, wherein said chemical coupling can be has been carried out by a chemical coupling means selected from the group consisting of comprising carbodiimide and or formaldehyde.

Claim 1603 (CURRENTLY AMENDED). The process according to claim 1601, wherein said enzymatic coupling ean be <u>has been</u> carried out by an enzymatic coupling means selected from the group consisting of comprising DNA ligase and or RNA ligase.

Claim 1604 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said incorporation comprises nick translation.

Claim 1605 (PREVIOUSLY PRESENTED). The process according to claim 1582 or 1604, wherein said incorporation is carried out by means of a polymerizing enzyme.

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Claim 1606 (PREVIOUSLY PRESENTED). The process according to claim 1605, wherein said polymerizing enzyme comprises a polymerase.

Claim 1607 (CURRENTLY AMENDED). The process according to claim 1606, wherein said polymerase is selected from the group consisting of comprises DNA polymerase and or RNA polymerase.

Claim 1608 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said one or more detectable non-radioactive chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate.

Claim 1609 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said incorporating step is template dependent or template independent.

Claim 1610 (PREVIOUSLY PRESENTED). The process according to claim 1609, wherein said incorporating step is template dependent.

Claim 1611 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one internal modified nucleotide.

Claim 1612 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide.

Claim 1613 (PREVIOUSLY CANCELED).

Claim 1614 (CURRENTLY AMENDED). The process according to claim 1582, wherein PM is selected from the group consisting of comprises a monophosphate, a di-phosphate, a tri-phosphate and or a tetra-phosphate.

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Claim 1615 (CURRENTLY AMENDED). The process according to claim 1582, wherein any of said nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claim 1616 (CANCELED).

Claim 1617. (CANCELED).

Claim 1618 (CURRENTLY AMENDED). The process according to claim 1616 1582, wherein SM is selected from the group consisting of comprises ribose, 2'-deoxyribose, 3'deoxyribose, and or 2',3'- dideoxyribose.

Claim 1619 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) and Sig is covalently attached to BASE at a <u>position when BASE</u> is a <u>pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and <u>or combinations thereof when BASE is a pyrimidine or is covalently attached to BASE at a <u>position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and <u>or combinations thereof when BASE is a purine</u>.</u></u></u>

Claim 1620 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) and Sig is covalently attached to BASE at a position <u>selected from the group consisting</u> of <u>comprising</u> the N<sup>4</sup> position when said pyrimidine comprises cytosine, the N<sup>2</sup> position when said purine comprises adenine or deazaadenine, the N<sup>6</sup> position when said purine comprises guanine, or deazaaguanine, and or combinations thereof.

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Claim 1621 (CURRENTLY AMENDED). The process according to claim 1582, wherein BASE in nucleotide <u>structures</u> or nucleotide analog structures (i), (ii) or (iii) is a 7-deazapurine.

Claim 1622 (PREVIOUSLY CANCELED).

Claim 1623 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) in which Sig is covalently attached to BASE through a linkage group.

Claim 1624 (PREVIOUSLY PRESENTED). The process according to claim 1623, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1625 (PREVIOUSLY PRESENTED). The process according to claim 1623, wherein said linkage group contains an amine.

Claim 1626 (PREVIOUSLY PRESENTED). The process according to claim 1625, wherein said amine comprises a primary amine.

Claim 1627 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (ii) in which Sig is covalently attached to SM through a linkage group.

Claim 1628 (PREVIOUSLY PRESENTED). The process according to claim 1627, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1629 (PREVIOUSLY CANCELED).

Claim 1630 (PREVIOUSLY CANCELED).

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Claim 1631 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (iii) in which Sig is covalently attached to PM through a linkage group.

Claim 1632 (PREVIOUSLY PRESENTED). The process according to claim 1631, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1633 (PREVIOUSLY CANCELED).

Claim 1634 (PREVIOUSLY CANCELED).

Claim 1635 (CURRENTLY AMENDED). The process according to claim 1582 1617, wherein the nucleotide structure or nucleotide analog structure is nucleotide structure or nucleotide analog structure (ii), and wherein PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine, or the N9 position when BASE is comprises a purine or, 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1636 (CURRENTLY AMENDED). The process according to claim 1582 1617, wherein the nucleotide structure or nucleotide analog structure is nucleotide structure or nucleotide analog structure (iii), and wherein PM is attached to SM at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine, or the N9 position when BASE is a purine or, 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

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Claim 1637 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (iii), and wherein said covalent attachment in nucleotide <u>structure</u> or nucleotide analog structure (iii) <u>is selected from the group consisting of comprises</u>

Claim 1638 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (iii), and wherein PM is <u>comprises</u> a mono-, di or tri-phosphate, and the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1639 (CURRENTLY AMENDED). The process according to claim 1582, wherein said covalent attachment in any of <u>said nucleotide structures</u> or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claim 1640 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide structure or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog

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structure (i) and said covalent attachment in comprises a member selected from the group consisting of: a — $CH_2NH$ — moiety, an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or both.

Claim 1641 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) and said covalent attachment comprises an allylamine group.

Claim 1642 (CURRENTLY AMENDED). The process according to claim 1582, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) and said covalent attachment in comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide <u>structure</u> or nucleotide analog structure (i), or any of the moieties

$$-CH = CH_2 - NH_-,$$
 $-CH = CH - CH_2 - NH_-,$ 
 $-CH = CH - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH = CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_- NH_-,$ 
 $-CH_2 - CH_2 -$ 

Claim 1643 (CURRENTLY AMENDED). The process according to claim 1582, wherein said covalent attachment in any of <u>said nucleotide structures</u> or nucleotide analog structures (i), (ii) or (iii) <u>includes comprises</u> a glycosidic linkage moiety.

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Claim 1644 (CURRENTLY AMENDED). The process according to claim 1582, wherein in <u>any of said nucleotide structures</u> or nucleotide analog structures (i), (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1645 (CURRENTLY AMENDED). The process according to claim 1644, wherein the nucleotide <u>structure</u> or nucleotide analog structure is nucleotide <u>structure</u> or nucleotide analog structure (i) and said linkage group contains an amine.

Claim 1646 (PREVIOUSLY PRESENTED). The process according to claim 1645, wherein said amine comprises a primary amine.

Claim 1647 (PREVIOUSLY PRESENTED). The process according to claim 1645, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1648 (PREVIOUSLY CANCELED).

Claim 1649 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least one double bond.

Claim 1650 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

Claim 1651 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

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Claim 1652 (PREVIOUSLY PRESENTED). The process according to claim 1651, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1653 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1654 (PREVIOUSLY PRESENTED). The process according to claim 1653, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1655 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1656 (CURRENTLY AMENDED). The process according to claim 1582, wherein said Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and or a chelating component or any combination of any of the foregoing.

Claim 1657 (CANCELED).

Claim 1658 (CURRENTLY AMENDED). The process according to claim 1657 1656, wherein said electron dense component comprises ferritin.

Claim 1659 (CANCELED).

Claim 1660 (CURRENTLY AMENDED). The process according to claim 1659 1656, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

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Claim 1661 (CURRENTLY AMENDED). The process according to claim 1659 1656, wherein said magnetic component comprises magnetic beads.

Claim 1662 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

Claim 1663 (PREVIOUSLY PRESENTED). The process according to claim 1662, wherein the binding protein comprises a lectin.

Claim 1664 (PREVIOUSLY PRESENTED). The process according to claim 1663, wherein the lectin comprises concanavalin A.

Claim 1665 (PREVIOUSLY PRESENTED). The process according to claim 1663, wherein said lectin is conjugated to ferritin.

Claim 1666 (PREVIOUSLY PRESENTED). The process according to claim 1656, wherein said Sig comprises an enzyme.

Claim 1667 (CURRENTLY AMENDED). The process according to claim 1666, wherein said enzyme is selected from the group consisting of comprises alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase, and peroxidase, or a combination thereof.

Claim 1668 (CANCELED).

Claim 1669 (CANCELED).

Claim 1670 (CURRENTLY AMENDED). The process according to claim 1669 1656, wherein said metal-containing component is catalytic.

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Claim 1671 (CURRENTLY AMENDED). The process according to claim 1582, wherein Sig emprises is a non-radioactively detectable indicator moiety molecule.

Claim 1672 (CURRENTLY AMENDED). The process according to claim 1671, wherein said indicator moiety molecule comprises an aromatic structure.

Claim 1673 (PREVIOUSLY PRESENTED). The process according to claim 1672, wherein said aromatic structure is heterocyclic.

Claim 1674 (PREVIOUSLY PRESENTED). The process according to claim 1673, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1675 (CURRENTLY AMENDED). The process according to claim 1674, wherein the fluorescent heterocyclic aromatic structure is selected from the group consisting of comprises fluorescein, rhodamine, and dansyl or any combination thereof.

Claim 1676 (PREVIOUSLY PRESENTED). The process according to claim 1675, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1677 (CURRENTLY AMENDED). The process according to claim 1671, wherein said indicator moiety molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and or a combination of any of the foregoing.

Claim 1678 (CANCELED).

Claim 1679 (CURRENTLY AMENDED). The process according to claim 1678 1677, wherein said fluorescent component is selected from the group consisting of comprises fluorescein, rhodamine and or dansyl.

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Claim 1680 (PREVIOUSLY PRESENTED). The process according to claim 1679, wherein said fluorescent component comprises fluorescein.

Claim 1681 (CANCELED).

Claim 1682 (PREVIOUSLY PRESENTED). The process according to claim 1656, wherein said Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

Claim 1683 (CANCELED).

Claim 1684 (CANCELED).

Claim 1685 (CURRENTLY AMENDED). The process according to claim 1582, wherein any of said nucleotide structures or nucleotide analogs structures (i), (ii) and (iii) are detectable by a means selected from the group consisting of comprising a fluorescent measurement, and a chemiluminescent measurement, or a combination thereof.

Claim 1686 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

Claim 1687 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group.

Claim 1688 (PREVIOUSLY PRESENTED). The process according to claim 1687, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

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Claim 1689 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest is terminally ligated or attached to a polypeptide.

Claim 1690 (PREVIOUSLY PRESENTED). The process according to claim 1689, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

Claim 1691 (PREVIOUSLY PRESENTED). The process according to claim 1689, wherein the polypeptide comprises a polylysine.

Claim 1692 (CURRENTLY AMENDED). The process according to claim 1689, wherein the polypeptide comprises at least one member-selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1693 (PREVIOUSLY PRESENTED). The process according to claim 1690, wherein said Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1694 (CURRENTLY AMENDED). The process according to claim 1690, wherein the said moiety which can be detected when the complex is formed is selected from the group consisting of comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chelating component or a combination of any of the foregoing.

Claim 1695 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being directly detected.

Claim 1696 (CURRENTLY AMENDED). The process according to claim 1695, wherein said directly detectable signal providing Sig detectable non-radioactive moiety is selected from the group

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eonsisting of comprises a fluorogenic structure, a chromogenic structure, a chemiluminescent structure, an electron dense structure and or an enzyme.

Claim 1697 (PREVIOUSLY PRESENTED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being indirectly detected.

Claim 1698 (CURRENTLY AMENDED). The process according to claim 1697, wherein <u>in said</u> detecting step, the indirectly detectable signal is provided by a <u>member selected from the group eonsisting of</u> an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme and <u>or</u> a combination of any of the foregoing.

Claim 1699 (CURRENTLY AMENDED). The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is eapable of being detected by a member selected from the group eonsisting of a means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

Claim 1700 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest; providing a metal or metal ion;

providing or generating non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs <u>has been ean be</u> attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating <u>said</u> a metal or metal ion and providing a detectable signal, and wherein said modified or labeled nucleotides or <u>modified</u>

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<u>or labeled</u> nucleotide analogs have been modified or labeled on at least one of the furanose furanosyl moiety, the phosphate moiety, or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting the presence of each of said separated or resolved fragments by detecting the signal provided by <u>said a metal or metal ion chelated</u> by said chelating structure or chelating components; and

determining the sequence of said nucleic acid of interest.

Claim 1701. (CURRENTLY AMENDED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest; providing a metal or metal ion;

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said a metal or metal ion and providing a detectable signal, and wherein said detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof;

introducing or subjecting said fragments to a sequencing gel; separating or resolving said fragments in said sequencing gel; and

detecting each of the separated or resolved fragments by detecting the signal provided by a said metal or metal ion chelated by said chelating structure or chelating components in the modified or labeled nucleotides or modified or labeled nucleotide analogs; and

determining the sequence of said nucleic acid of interest.

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Claim 1702. (CURRENTLY AMENDED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest;

poviding a metal or metal ion;

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs ean be has been attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said a metal or metal ion and providing a detectable signal, and wherein said detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof;

detecting with a sequencing gel the detectable non-radioactive labeled nucleic acid fragments by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating components; and

determining the sequence of said nucleic acid of interest.

Claim 1703. (CURRENTLY AMENDED) A process for determining the sequence of a nucleic acid of interest, comprising detecting with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating a said metal or metal ion and providing a detectable signal, and wherein said modified or labeled

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nucleotides or <u>modified or labeled</u> nucleotide analogs have been modified or labeled on at least one of the <u>furanose</u> <u>furanosyl</u> moiety, the phosphate moiety, or any combination thereof.

Claim 1704. (CURRENTLY AMENDED) A process for determining in a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid sequence of interest or a portion thereof, said process comprising:

- (A) providing a sample which may comprise a nucleic acid of interest;
- (B) providing a metal or metal ion;
- (C) providing
- (1) one or more detectable non-radioactive chemically modified or chemically labeled nucleotides or detectable non-radioactive chemically modified or chemically labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid, or
- (2) one or more oligonucleotides or polynucleotides comprising at least one of said nucleotides or nucleotide analogs ( $i\underline{1}$ ); or
  - (3) both (1) and (2);

wherein said nucleotides or nucleotide analogs (1) and said oligonucleotides and polynucleotides (2) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, wherein said nucleotides or nucleotide analogs (1) comprise one or more chelating structures or chelating components capable of chelating a said metal or metal ion and providing a detectable signal, and wherein said nucleotides or nucleotide analogs (1) have been non-radioactively modified or non-radioactively labeled, non-disruptively or disruptively, on at least one of the furanose furanosyl moiety, the phosphate moiety, or the base moiety, or any combination thereof; and

(<u>BD</u>) incorporating said nucleotides or nucleotide analogs (1) or said oligonucleotides or polynucleotides (2), or both (1) and (2), into said nucleic acid fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, and wherein said nucleotides or nucleotide analogs (1) comprise a detectable non-radioactive chemically

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modified or labeled nucleotide structure, or detectable non-radioactive chemically modified or labeled nucleotide analog structure, selected from the group consisting of one or more of :

wherein B represents comprises a purine moiety, a 7-deazapurine moiety, or a pyrimidine moiety, and B is covalently bonded to the C1'-position of the furanose furanosyl moiety provided that whenever B is a purine or a 7-deazapurine moiety, the furanose furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanose furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety comprising a chelating structure or chelating component capable of chelating a said metal or metal ion and providing directly or indirectly a detectable signal; and

wherein B and A are covalently attached directly or through a linkage group, and wherein x comprises a member selected from the group consisting of:

wherein y comprises a member selected from the group consisting of:

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wherein z comprises a member selected from the group consisting of

H- and HO-

(ii)

## wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and <u>or</u>

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety,

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal; and

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wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

- $(\underline{\mathbf{CE}})$  transferring or subjecting said labeled fragments to a sequencing gel;
- (DF) separating or resolving said labeled fragments; and
- $(\underline{EG})$  detecting directly or indirectly the presence of said labeled fragments by means of a metal or metal ion chelated by said chelating structure or chelating components.

Claim 1705 (CURRENTLY AMENDED). A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (a) providing a sample which may comprise a nucleic acid of interest;
- (b) providing a metal or metal ion;
- specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:
  - (i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

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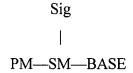
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SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a signalling moiety comprising a chelating structure or component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-deazapurine moiety, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide structure or nucleotide analog structure having the formula



## wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or component capable of providing chelating a <u>said</u> metal or metal ion and a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and <u>or</u>

(iii) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or components capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2', 3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(bd) detecting the presence of Sig in any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating components.

Claim 1706 (CURRENTLY AMENDED). A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (A) providing:
  - (i) an oligo- or polynucleotide having two segments:
  - (a) a first segment complementary to and capable of hybridizing to a portion of said nucleic acid of interest; and
    - (b) a second segment comprising at least one protein binding sequence; and

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## (ii) a metal or metal ion;

- (iii) a detectable protein capable of binding to said protein binding sequence and comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal;
- (B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide and said detectable protein (ii) to form a complex;
- (C) detecting the presence of said protein in said complex and said nucleic acid of interest by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating component.

Claim 1707. (CURRENTLY AMENDED) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising:

providing a cell;

providing a metal or metal ion;

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula

PM—SM—BASE—Sig

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and or

(iii) a nucleotide structure or nucleotide analog structure having the formula

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wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating component, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome; and

determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1708 (CURRENTLY AMENDED). A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising:

providing a cell;

providing a metal or metal ion;

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or

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detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,
SM is a furanose furanosyl moiety,
BASE is a base moiety, and

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Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and <u>or</u>

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

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identifying said chromosome of interest by means of said hybridization pattern obtained.

Claim 1709 (CURRENTLY AMENDED). A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising:

providing a cell of interest;

providing a metal or metal ion;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator moiety and each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA and wherein each set comprises a different indicator molecule, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

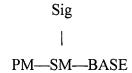
BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to

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SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a said metal or metal ion and providing a detectable signal, wherein Sig comprises at

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least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying <del>any one</del> <u>a plurality or all</u> of the chromosomes in said cell of interest.

Claim 1710 (CURRENTLY AMENDED). A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

providing an interphase cell of interest;

providing a metal or metal ion;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analog comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:

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(i) a nucleotide structure or nucleotide analog structure having the formula

wherein

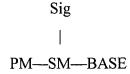
PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a, pyrimidine moiety, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and <u>or</u>

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(iii) a nucleotide structure or nucleotide analog structure having the formula

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting by means of a <u>said</u> metal or metal ion chelated by said chelating structure or chelating component any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Claim 1711 (CURRENTLY AMENDED). A process for preparing a labeled oligo- or polynucleotide of interest, comprising:

- (A) providing a metal or metal ion;
- (B) providing either:

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- (1) one or more detectable chemically modified or labeled nucleotides or detectable chemically modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more signalling moieties comprising a chelating structure or chelating component capable of chelating a metal or metal ion and providing a detectable signal, or
- (2) an oligo- or polynucleotide of interest comprising one or more of said modified or labeled nucleotides or modified or labeled nucleotide analogs (1), alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, or
  - (3) both (1) and (2).

wherein said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs (1) are modified on at least one of the <u>furanose furanosyl</u> moiety, the phosphate moiety, or the base moiety or any combination thereof, and wherein the modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs comprise a nucleotide structure or nucleotide analog structure selected from the group consisting of one or more of comprising:

(i)

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

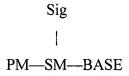
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

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Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii)



wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a signal, wherein Sig comprises at least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and <u>or</u>

(iii)

wherein

PM is a phosphate moiety,

SM is a furanose furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating a <u>said</u> metal or metal ion and providing a detectable signal; wherein Sig comprises at least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or

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a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and said oligo- or polynucleotide of interest; and

( $\underline{BC}$ ) either incorporating said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

Claim 1712 (CURRENTLY AMENDED). A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing a sample which may contain a nucleic acid of interest;

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotides or polynucleotides, each of said detectable non-radioactively labeled oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the moiety, the phosphate moiety, or the base moiety, and (ii) a sample that may contain said nucleic acid of interest;

forming in liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest;

separating or resolving in a gel said formed hybrids; and

detecting non-radioactively the separated or resolved hybrids to detect the presence of said nucleic acid of interest.

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Claim 1713 (CURRENTLY AMENDED). The process according to claim 1712, wherein after said hybrid forming step, the liquid phase is subjected to nuclease treatment further comprising after said hybrid forming step, the step of subjecting the liquid phase to nuclease treatment.

Claim 1714 (CURRENTLY AMENDED). The process according to claim 1712, wherein said nucleic acid of interest is selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1715 (CURRENTLY AMENDED). The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides are selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1716 (CURRENTLY AMENDED). The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise a member selected from the group eonsisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, and a chelating component or a combination of any of the foregoing.

Claim 1717 (PREVIOUSLY PRESENTED). The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly.

Claim 1718 (CURRENTLY AMENDED). The process according to claim 1712, wherein said detecting step is carried out by means of a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chromogenic measurement, a chemiluminescent measurement, a microscopic measurement and or an electron density measurement.

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Claim 1719 (CURRENTLY AMENDED). The process according to claim 569, wherein said nucleic acid of interest is selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1720 (CURRENTLY AMENDED). The process according to claim 721, wherein said nucleic acid of interest is selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1721 (CURRENTLY AMENDED). The process according to claim 873, wherein said nucleic acid of interest is selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1722 (CURRENTLY AMENDED). The process according to claim 1025, wherein said nucleic acid of interest is selected from the group consisting of comprises DNA, RNA and or DNA-RNA.

Claim 1723 (CURRENTLY AMENDED). The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with the same indicator moieties molecules.

Claim 1724 (CURRENTLY AMENDED). The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with different indicator moieties molecules.

Claim 1725 (CURRENTLY AMENDED). The process according to claim 1400, wherein said direct detection is carried out with the same indicator moieties molecules.

Claim 1726 (CURRENTLY AMENDED). The process according to claim 1400, wherein said direct detection is carried out with different indicator moieties molecules.

Claim 1727 (PREVIOUSLY PRESENTED). The process according to claim 1712, wherein said detecting step comprises localizing said separated or resolved hybrids.

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Claim 1728 (PREVIOUSLY PRESENTED). The process of any of claims 1700, 1701, 1702 or 1704, wherein in said providing step, the chelating structure or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1729 (CURRENTLY AMENDED). The process of claim 1703, wherein <u>in</u> said detecting step, the chelating structure or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminesscent, electron dense or magnetic.

Claim 1730 (CURRENTLY AMENDED). The process of claim 1705, wherein <u>in</u> said specific hybridizing step, the chelating structure or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1731 (CURRENTLY AMENDED). The process of claim 1707, wherein <u>in</u> said contacting step, the chelating structure or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1732 (PREVIOUSLY PRESENTED). The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein said detecting step is carried out by a structure or component that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1733 (CURRENTLY AMENDED). The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein in said detecting step, the chelating structure or chelating components have chelated a <u>said</u> metal or metal ion selected from the group consisting of <u>comprising</u> heavy metals, and rare earth metals, or both.

Claim 1734 (PREVIOUSLY PRESENTED). The process of claim 1733, wherein said heavy metal comprises cobalt.

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Claim 1735 (PREVIOUSLY PRESENTED). The process of claim 1732, wherein said detecting step is carried out radioactively.

Claim 1736 (PREVIOUSLY PRESENTED). The process of claim 1735, wherein said radioactive detection is carried out by means of an isotope.

Claim 1737 (PREVIOUSLY PRESENTED). The process of claim 1736, wherein said isotope is a  $\beta$  or  $\gamma$  emitter.

Claim 1738 (CURRENTLY AMENDED). The process of claim 1735, wherein said radioactive detection is carried out with an isotope selected from the group consisting of comprising bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 and or yttrium-90.

Claim 1739 (CURRENTLY AMENDED) The process of any of claims 638, 640, 674, 676, 790, 792, 826, 828, 942, 944, 978, 980, or 1094, 1096, 1130 or 1132, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

Claim 1740 (CURRENTLY AMENDED). The process of any of claims 657, 693, 809, 845, 961, 997, 1113, 1149, or 1287, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are labeled with the same indicator moieties molecules.

Claim 1741 (CURRENTLY AMENDED). The process of any of claims 657, 693, 809, 845, 961, 997, 1113, 1149, or 1287, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are labeled with different indicator moieties molecules.

Claim 1742 (CURRENTLY AMENDED). The process of any of claims 583, 735, 887 or 1039, wherein said primers or said nucleoside triphosphates are labeled.

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Claim 1743 (CURRENTLY AMENDED). The process of any of claims 569, 721, 873, 1025, 1177, 1700, 1701, 1702, 1703 or 1704, wherein said base is a pyrimidine analog or a purine analog.

Claim 1744 (CURRENTLY AMENDED). The process of claim 1743, wherein said pyrimidine analogs selected from the group consisting of comprise thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs and deoxycytidine analogs.

Claim 1745 (CURRENTLY AMENDED). The process of claim 1744, wherein said uridine <u>analog</u> comprises 5-bromo-2'-deoxyuridine-5'-phosphate.

Claim 1746 (CURRENTLY AMENDED). The process of claim 1744, wherein said deoxycytidine analog comprises 5-hydroxymethyl-2'-deoxycytidylic acid.

Claim 1747 (CURRENTLY AMENDED). The process of claim 1743, wherein said purine <u>analogs</u> is selected from the group consisting of <u>comprise</u> adenosine <u>analogs</u>, deoxyadenosine <u>analogs</u>, guanosine <u>analogs</u> and <u>or</u> deoxyguanosine <u>analogs</u>.

Claim 1748 (CURRENTLY AMENDED). The process of claim 1747, wherein said adenosine analogs is selected from the group consisting of comprise tubericidin and or toyocamycin.

Claim 1749 (PREVIOUSLY PRESENTED). The process of any of claims 1706, 1708, 1709, 1710 or 1711, wherein in said providing step, the chelating structure or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1750 (CURRENTLY AMENDED). The process of any of claims 1705, 1706, 1707, 1708, 1709, or 1710 or 1711, wherein said detecting step is carried out by a structure or component that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

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Claim 1751 (CURRENTLY AMENDED). The process of any of claims 1705, 1706, 1707, 1708, 1709, or 1710-or 1711, wherein in said detecting step, the chelating structure or chelating components have a chelated a metal or metal ion selected from the group consisting of comprising heavy metals and or rare earth metals.

Claim 1752 (PREVIOUSLY PRESENTED). The process of claim 1751, wherein said heavy metal comprises cobalt.

Claim 1753 (PREVIOUSLY PRESENTED). The process of claim 1750, wherein said detecting step is carried out radioactively.

Claim 1754 (PREVIOUSLY PRESENTED). The process of claim 1753, wherein said radioactive detection is carried out by means of an isotope.

Claim 1755 (PREVIOUSLY PRESENTED). The process of claim 1754, wherein said isotope is a  $\beta$  or  $\gamma$  emitter.

Claim 1756 (CURRENTLY AMENDED). The process of claim 1753, wherein said radioactive detection is carried out with an isotope selected from the group consisting of comprising bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 and or yttrium-90.

Claim 1757 (PREVIOUSLY PRESENTED). The process of any of claims 1354, 1356, 1450, 1452, 1512, 1514, 1652 or 1654, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

Claim 1758 (CURRENTLY AMENDED). The process of claims 1373 or 1671, wherein said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs are labeled with the same indicator <del>moieties</del> molecules.

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Claim 1759 (CURRENTLY AMENDED). The process of claims 1373 or 1671, wherein said modified or labeled nucleotides or <u>modified or labeled</u> nucleotide analogs are labeled with different indicator <u>moieties</u> <u>molecules</u>.

Claim 1760 (CURRENTLY AMENDED). The process of any of claims 1298, 1473, 1474, 1475, 1476, 1582, 1705, 1706, 1707, 1708, 1709, 1710, or 1711 or 1712, wherein said base is comprises a pyrimidine analog or a purine analog.

Claim 1761 (CURRENTLY AMENDED). The process of claim 1760, wherein said pyrimidine analogs is selected from the group consisting of comprise thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs and or deoxycytidine analogs.

Claim 1762 (CURRENTLY AMENDED). The process of claim 1761, wherein said uridine analogs comprises comprise 5-bromo-2'-deoxyuridine-5'-phosphate.

Claim 1763 (CURRENTLY AMENDED). The process of claim 1761, wherein said deoxycytidine analogs comprise comprises 5-hydroxymethyl-2'-deoxycytidylic acid.

Claim 1764 (CURRENTLY AMENDED). The process of claim 1760, wherein said purine <u>analog</u> is selected from the group consisting of <u>comprises</u> adenosine <u>analogs</u>, deoxyadenosine <u>analogs</u>, guanosine <u>analogs</u> and <u>or</u> deoxyguanosine <u>analogs</u>.

Claim 1765 (CURRENTLY AMENDED). The process of claim 1764, wherein said adenosine analogs is selected from the group consisting of comprise tubericidin and or toyocamycin.

Claim 1766 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest, comprising:

providing at least one nucleic acid of interest;

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion

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thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides;

subjecting said detectable <del>non-radioactively</del> labeled fragments to a sequencing gel to separate or resolve said fragments; <del>and</del>

detecting non-radioactively the presence of each of said separated or resolved fragments by detecting the modified or non-radioactively modified or labeled nucleotides; and

determining the sequence of said nucleic acid of interest.

Claim 1767 (CURRENTLY AMENDED). A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein each of said fragments comprises one or more nucleotides, and wherein said one or more nucleotides comprise one or more fluorescent, chromogenic or chemiluminescent indicators on at least one of the furanose furanosyl moiety, the phosphate moiety or the base moiety or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively each of said separated or resolved fragments by detecting the fluorescent, chromogenic or chemiluminescent indicators.

Claim 1768 (CURRENTLY AMENDED). A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that ean <u>may</u> be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent or chromogenic indicators are covalently attached, directly or through a linkage group, to at least one of the <u>furanose furanosyl</u> moiety, the phosphate moiety, or the base moiety of said nucleotides, or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

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detecting non-radioactively each of said separated or resolved fragments by means of the said fluorescent or chromogenic indicators attached to said nucleotides.

Claim 1769 (CURRENTLY AMENDED). A process for determining the sequence of a nucleic acid of interest comprising:

providing at least one nucleic acid of interest;

generating detectable non-radioactively labeled nucleic acid fragments complementary to said nucleic acid of interest or a portion thereof, wherein said fragments have been labeled by incorporation of one or more detectable non-radioactive modified or labeled nucleoside triphosphates, said nucleoside triphosphates comprising fluorescent or chemiluminescent chromogenic indicators;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting each of said separated or resolved fragments by means of the <u>said</u> fluorescent or <u>chemiluminescent</u> <u>chromogenic</u> indicators, to determine the sequence of said nucleic acid of interest.

Claim 1770 (CURRENTLY AMENDED). The process according to claim 1769, wherein in said generating step, said modified or labeled nucleoside triphosphates comprise a <u>furanose</u> <u>furanosyl</u> moiety.

Claim 1771 (CURRENTLY AMENDED). The process according to claim 1770, wherein said furanose furanosyl moiety comprises a ribose, 2'-deoxyribose, 3'-deoxyribose or 2',3'-dideoxyribose.

Claim 1772 (PREVIOUSLY PRESENTED). The process according to claim 1769, wherein in said generating step, said one or more detectable non-radioactive modified or labeled nucleoside triphosphates comprise a phosphate moiety.

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Claim 1773 (CURRENTLY AMENDED). The process according to claim 1769, wherein in said generating step, said modified or labeled nucleoside triphosphates comprise <u>a base moiety or a base analog comprising</u> a purine, a purine analog, a 7-deazapurine, a 7-deazapurine <u>analog</u>, <del>or</del> a pyrimidine, or a pyrimidine analog.

Claim 1774 (PREVIOUSLY CANCELED).

Claim 1775 (CURRENTLY AMENDED). The process according to claim 1773, wherein the fluorescent or chemiluminescent indicators in said modified or labeled nucleoside triphosphates are attached to said purine, said purine analog, said 7-deazapurine, said 7-deazapurine analog, of said pyrimidine, or said pyrimidine analog.

Claim 1776 (NEW). A process for determining the sequence of a nucleic acid of interest, comprising:

providing at least one nucleic acid of interest;

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof;

subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments;

detecting non-radioactively the presence of said separated or resolved fragments; and determining the sequence of said nucleic acid of interest.

Claim 1777 (NEW). A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments; subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments.

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Claim 1778 (NEW). A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein said fragments comprise one or more detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, or the base moiety or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by detecting said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Claim 1779 (NEW). A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein said fragments comprise one or more detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by detecting said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Claim 1780 (NEW). A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

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detecting non-radioactively said separated or resolved fragments by means of said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Claim 1781 (NEW). A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, or the base moiety or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by means of the modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1782 (NEW). A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein each of said fragments comprises one or more nucleotides, and wherein said one or more nucleotides comprise one or more fluorescent, or chromogenic indicators;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by detecting the fluorescent, or chromogenic indicators.

Claim 1783 (NEW). A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that can be attached to, or coupled to, or incorporated into DNA

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or RNA, and wherein one or more fluorescent or chromogenic indicators are covalently attached, directly or through a linkage group, to said one or more nucleotides;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by means of said fluorescent or chromogenic indicators attached to said one or more nucleotides.

Claim 1784 (NEW). A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotide or polynucleotide, each of said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to, coupled to, or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest;

forming liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest; subjecting said liquid phase to nuclease treatment; and detecting the hybrids non-radioactively to detect the presence of said nucleic acid of interest.

1785. (NEW). A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) a detectable non-radioactively labeled oligonucleotide or polynucleotide, said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotide or polynucleotide comprises one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which

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nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest; and

detecting hybrids non-radioactively to detect the presence of said nucleic acid of interest.

Claim 1786. (NEW) The process according to claim 1785, further comprising a treatment that acts upon a non-hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide and leaves a hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide intact.

Claim 1787. (NEW) The process according to claim 1786 wherein said treatment is a nuclease treatment.

Claim 1788. (NEW) The process according to claim 1784 or 1787 wherein said nuclease treatment is carried out by S1 nuclease, Exonuclease I from *E.coli*, or a combination thereof.

Claim 1789. (NEW) The lprocess according to any of claims 1784, 1785, 1786 or 1787 further comprising separating or resolving in a gel said formed hybrids.

Claim 1790 (NEW). The process according to claim 1784 or 1785, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1791 (NEW). The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises DNA, RNA or DNA-RNA.

Claim 1792 (NEW). The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or a combination of any of the foregoing.

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Claim 1793 (NEW). The process according to claim 1784 or 1785, wherein said non-radioactive detection step is carried out directly or indirectly.

Claim 1794 (NEW). The process according to claim 1784 or 1785, wherein said detecting step is carried out by means of an enzymatic measurement, a fluorescent measurement, a chromogenic measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

\* \* \* \* \* \* \*

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### REMARKS

Reconsideration of this application is respectfully requested.

A complete listing of the claims in this application is provided above. The complete listing identifies claims that are currently amended, claims that were previously presented, claims that have been canceled by this paper, and claims that were previously canceled.

# Status of Claims After Entry

After entry of the claims identified in the complete listing above, the status of the claims will be as follows:

Amended claims: 569, 570, 571, 573, 575, 577, 582-584, 586-589, 592, 594, 597-600, 602-604, 607-608, 610-612, 614-622, 634-635, 637, 641-642, 646, 648, 656-658, 661, 667, 670, 707, 709-711, 713-714, 716-717, 719-721, 723, 725-727, 729, 734-736, 739-740, 744-747, 751-752, 754-756, 759-760, 762-764, 766-774, 786-787, 789, 793-794, 796-797, 800, 808-810, 813, 819, 822, 859, 861-863, 865-866, 868-869, 871-873, 875, 877, 879, 881, 886-888, 891-892, 895-899, 902-904, 906-908, 911-912, 914-916, 918-926, 938-939, 941, 945-947, 949, 952, 960-962, 965, 971, 974, 1011, 1013-1018, 1020-1021, 1023-1025, 1027, 1029, 1031, 1033, 1038, 1040, 1043-1044, 1047-1050, 1054-1056, 1058-1060, 1063-1064, 1066-1068, 1070-1078, 1090-1091, 1093, 1097-1099, 1101, 1104, 1112-1114, 1117, 1123, 1126, 1163, 1165-1167, 1169-1170, 1172-1173, 1175-1177, 1179, 1181, 1183, 1185, 1190, 1197-1198, 1208-1209, 1212-1216, 1218, 1220, 1222, 1224, 1226, 1228, 1230-1240, 1249, 1253, 1263-1265, 1268, 1270, 1272, 1275, 1278-1279, 1282, 1283, 1287, 1288, 1291-1292, 1294, 1297-1298, 1303, 1304, 1307-1309, 1311-1312, 1318, 1320-1322, 1326-1328, 1331-1332, 1334-1346, 1358, 1360, 1362-1363, 1369, 1372-1374, 1377, 1380, 1383, 1386-1387, 1391, 1395-1396, 1398, 1400-1401, 1404-1407, 1409, 1410, 1411 1416-1417, 1420-1422, 1425, 1427, 1430, 1432, 1433, 1436-1442, 1444-1449, 1451, 1453-1455, 1458, 1460-1462, 1467-1468, 1470-1471, 1473-1476, 1479-1481, 1485-1487, 1490-1491, 1493-1505, 1516, 1520-1521, 1522, 1527, 1530-1532, 1535, 1538, 1544-1546, 1550-1551, 1556-1557, 1559, 1561-1562, 1565, 1568, 1570, 1573, 1577-1579, 1582, 1585, 1587, 1592-1594, 1601-1603, 1607, 1614-1615, 1618-1621, 1623, 1627, 1631, 1635-1645, 1656, 1658, 1660-1661, 1667, 1670-1672, 1675, 1677,

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1679, 1685, 1692, 1694, 1696, 1698-1716, 1718-1726, 1729-1731, 1733, 1738-1748, 1750, 1751, 1756, 1758-1771, 1773 and 1775.

Canceled claims: 572, 576, 578-581, 590-591, 595, 601, 605-606, 613, 625-633, 636, 639-640, 643, 645, 654-655, 662-666, 668-669, 671-679, 681-682, 684-687, 690-706, 724, 728, 730-733, 753, 757-758, 765, 777-785, 788, 791-792, 795, 806-807, 814-818, 820-821, 823-831, 833-834, 836-839, 842-858, 876, 880, 882-885, 905, 909-910, 913, 917, 929-937, 940, 943-944, 950, 958-959, 966-970, 972-973, 975-983, 985-986, 988-991, 994-1010, 1028, 1032, 1034-1037, 1057, 1061-1062, 1069, 1081-1089, 1092, 1095-1096, 1102, 1110-1111, 1118-1122, 1124-1125, 1127-1135, 1137-1138, 1140-1143, 1146-1162, 1180, 1184, 1186-1189, 1210, 1245-1247, 1250, 1252, 1261-1262, 1271, 1273-1274, 1276-1277, 1329, 1352, 1355-1356, 1359, 1361, 1370-1371, 1381-1382, 1384-1385, 1392, 1488, 1517, 1519, 1526, 1528-1529, 1540, 1542-1543, 1586, 1588-1591, 1616-1617, 1657, 1659, 1668-1669, 1678, 1681 and 1683-1684.

New claims added: 1776-1794.

Pending claims presented for further examination: 569-571, 573-575, 577, 582-589, 592-594, 597-600, 602-604, 607-608, 610-612, 614-624, 634-635, 637-638, 641-642, 646, 648-651, 656-661, 667, 670, 707-714, 716-717, 719-723, 725-727, 729, 734-747, 749-752, 754-756, 759-760, 762-764, 766-776, 786-787, 789-790, 793-794, 796-797, 800-803, 808-813, 819, 822, 859-866, 868-869, 871-875, 877-879, 881, 886-899, 901-904, 906-908, 911-912, 914-916, 918-928, 938-939, 941-942, 945-949, 952-955, 960-965, 971, 974, 1011-1018, 1020-1021, 1023-1027, 1029-1031, 1033, 1038-1051, 1053-1056, 1058-1060, 1063-1064, 1066-1068, 1070-1080, 1090-1091, 1093-1094, 1097-1099, 1101, 1104-1107, 1112-1117, 1123, 1126, 1163-1170, 1172-1173, 1175-1179, 1181-1183, 1185, 1190-1200, 1204, 1208-1209, 1212-1216, 1218-1244, 1248-1249, 1253, 1255-1258, 1263-1270, 1272, 1275, 1278-1294, 1296-1328, 1331-1332, 1334-1351, 1353-1354, 1357-1358, 1360, 1362-1369, 1372-1380, 1383, 1386-1391, 1393-1407, 1409-1487, 1490-1491, 1493-1516, 1518, 1520-1525, 1527, 1530-1539, 1541, 1544-1568, 1570-1585, 1587, 1592-1612, 1614-1615, 1618-1621, 1623-1628, 1631-1632, 1635-1647, 1649-1656, 1658, 1660-1667, 1670-1677, 1679-1680, 1682, 1685-1773 and 1775-1794.

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Before addressing the changes in the claims, Applicants would like to thank Examiner Ardin H. Marschel for the courtesy that he extended at the April 1, 2004 interview to Gene Rzucidlo, Esq., also of record in this case, Dr. James J. Donegan, Senior Scientist for Enzo Life Sciences, Inc., and their undersigned attorney.<sup>1</sup>

# **Changes to the Claims**

The changes to the claims include the following:

## **Furanosyl**

In any claim where reference was made to the "furanose moiety," the term has been changed to "furanosyl moiety." This matter was discussed at the April 1, 2004 interview where it was agreed that the term "furanosyl moiety" better describes the nature of the ring element in nucleic acid structure. Claims affected by this amendment include 569, 600, 721, 752, 904, 1025, 1056, 1177, 1298, 1473-1476, 1582, 1700-1705, 1707-1712, 1767-1768, and new claims 1778, 1781 and 1784.

## Nucleotide Analog

The matter of nucleotide analogs was also discussed at the April 1, 2004. Applicants' attorneys explained that the term "nucleotide analog" is a term long recognized in the art, as evidenced by the books authored by Prof. Dr. Karl Heinz Scheit [Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, New York, 1980], and Dr. Arthur Kornberg [DNA Synthesis, W. H. Freeman and Company, San Francisco, CA 1974; DNA Replication, also Freeman and Company, 1980; 1982 Supplement to DNA Replication, again, Freeman and Company]. Applicants' attorneys also pointed out that Kornberg's "nucleotide analogs" were defined as those molecules that could be incorporated into DNA or RNA. It was generally agreed that the term "nucleotide analog" could be recited in the claims, with additional embodiments or language directed to "base analogs," because Applicants' specification disclosed several examples of these.

<sup>&</sup>lt;sup>1</sup> This paper is largely a follow up to the April 1, 2004 interview. In the Interview Summary, it is indicated that "[w]e discussed a number of possible claim amendments to overcome the rejections of record."

<sup>&</sup>lt;sup>2</sup> These books are already of record in this application.

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Thus, many of the claims as amended or presented by this paper include the term "nucleotide analog," and some dependent claims recite "base analogs" and various related terms.

Wherever possible in referring to nucleotide analogs, Applicants have used the same corresponding descriptive language as for nucleotides. Thus, claim 569 recites "modified or labeled nucleotides or *modified or labeled nucleotide analogs*." This matter was also raised in the July 1, 2003 Office Action (page 9).

### Indicator Molecule

The nature of "indicator molecule" was also raised in the July 1, 2003 Office Action (pages 8-9). In order to clarify the relationship between the detectable non-radioactive moieties A or Sig and the indicator molecules, Applicants have amended several claims to recite that "said A or said Sig is a non-radioactively detectable indicator molecule." The claims affected by these clarifying amendments include 657, 809, 961, 1113, 1264, 1373, 1445, 1531, 1544 and 1671.

# Non-Nucleotidyl

At the April 1, 2004 interview, various pieces of prior art cited in the July 1, 2003 Office Action were discussed. Regarding the Dunn [Cell 12:23 (1977)] and Hartman [Biopolymers 20:2635 (1981)] documents, it was generally agreed that a description in the claims that the detectable non-radioactive moiety was *non-nucleotidyl* in nature, would probably overcome the prior art rejections. Thus, claims 1298 and 1582 have each been amended to recite "a detectable non-radioactive *non-nucleotidyl* moiety . . ." Because the Examiner urged a showing of support, Applicants respectfully point out that The inserted term -- non-nucleotidyl -- is supported by the specification. For example, members of the non-radioactive label moiety Sig are described on several pages in the specification. For example, on page 10, it is disclosed:

A may be any moiety which has at least three carbon atoms and is capable of forming a detectable complex with a polypeptide when the modified nucleotide is incorporated into a double-stranded duplex containing either deoxyribonucleic or ribonucleic acid. . . .

Of these preferred A moieties are biotin and iminobiotin.

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[emphasis added]<sup>3</sup>

See pages 96, last paragraph, continuing through page 97, first paragraph, and each of these members are non-nucleotidyl in nature:

The Sig moiety employed in the make-up of the special nucleotides of this invention could comprise an enzyme or enzymic material, such as alkaline phosphatase, glucose oxidase, horseradish peroxidase or ribonuclease. The Sig moiety could also contain a fluorescing component, such as fluorescein or rhodamine or dansyl. If desired, the Sig moiety could include a magnetic component associated or attached thereto, such as a magnetic oxide or magnetic iron oxide, which would make the nucleotide or polynucleotide containing such a magnetic-containing Sig moiety detectable by magnetic means. The Sig moiety might also include an electron dense component, such as ferritin, so as to be available by observation. The Sig moiety could also include a radiation detecting means. The Sig moiety might also include a hapten component or per se be capable of complexing with an antibody specific thereto. Most usefully, the Sig moiety is a polysaccharide or oligosaccharide or monosaccharide, which is capable of complexing with or being attached to a sugar or polysaccharide binding protein, such as a lectin, e.g. Concanavilin A. The Sig component or moiety of the special nucleotides in accordance with this invention could also include a chemiluminescent component. [emphasis added]<sup>4</sup>

With respect to claim 1411 in which the detection process is carried out with a non-radioactively detectable protein, it was generally agreed that the recitation of "operator sequence" in the claim would probably overcome the anticipation rejection by Kourilsky (P/N 4,581,333 and GB 2,019,408). At the April 1st interview, Applicants attorneys and representative indicated that "operator sequence" was being used in a classical sense, much as in Example XXXIV in the specification.

<sup>&</sup>lt;sup>3</sup> Biotin and iminobiotin are listed among the members for A and Sig in several dependent claims.

<sup>&</sup>lt;sup>4</sup> The boldfaced elements are also recited as members of Sig in several dependent claims.

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### Miscellaneous

In keeping up with a growing trend, Applicants have deleted the Markush language in the previous claims. See claim 571 ("wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, . . .") where the Markush language has been deleted in favor of other language ("wherein said organism comprises bacteria, fungi, viruses, yeast, mammals, . . .").

### Claim Cancellations

In drafting the claims presented above, Applicants have purposefully sought to reduce the number of claims. Thus, the structures for the base moieties labeled with A or Sig have been combined with the consequence of eliminating many dependent claims.

# New Claims

As indicated above, claims 1776-1794 have been added above. The new claims bear similarity to various claims already of record. Their entry is respectfully requested.

Entry of the above claim listing is respectfully requested.

# **Submission of New Request for Interference**

Applicants' attorneys are preparing a new request for interference that will be submitted shortly.